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FILE COVERS 1907 - 9 Mar 2005 VOL 142 ISS 11 FILE LAST UPDATED: 8 Mar 2005 (20050308/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L45 ANSWER 1 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
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- AN 2004:563390 HCAPLUS
- DN 141:122332
- ED Entered STN: 14 Jul 2004
- TI Amyloid  $\beta$  epitopes, chimeric polypeptides and anti-A $\beta$  antibodies for diagnosis and passive immunization treatment of Alzheimer's disease
- IN Schenk, Dale B.
- PA Neuralab Limited, Bermuda
- SO U.S., 79 pp.
  - CODEN: USXXAM
- DT Patent
- LA English

US 6761888

US 6750324

- IC ICM C07K016-00
  - ICS C07K016-18; A61K039-00
- NCL 424130100; 530300000; 530350000; 530387100
- CC 15-3 (Immunochemistry)

Section cross-reference(s): 9, 63

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A61K039/395

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PATENT NO.		KIND	DATE	AP	PLICATION NO.	DATE	
US 6761888		B1	20040713	US	2000-580018	20000526	
US 6750324		В1	20040615	US	2000-724552	20001128 <	
US 6787637		B1	20040907	US	2000-724551	20001128	
US 2004247	591	A1	20041209	US	2004-890070	20040712	
US 2004265	301	A1	20041230	US	2004-890000	20040712	
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US 1997-67	740P	P	19971202	<			
US 1998-80	970P	P	19980407	<			
US 1998-20	1430	A2	19981130	<			
US 1999-32	2289	A2	19990528				
US 2000-58	0018	A1	20000526				
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A61K038/17A2; A61K038/19B+M; A61K039/00D3;

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C07K014/47A3; C07K016/18
US 2004247591 ECLA
                        A61K039/395
US 2004265301 ECLA
                        A61K039/395
US 2004247590 ECLA
                        A61K039/395
    The invention provides improved agents and methods for treatment of
AB
    diseases associated with amyloid deposits of A\beta in the brain of a
    patient. Such methods entail administering agents that induce a
    beneficial immunogenic response against the amyloid deposit. The methods
     are useful for prophylactic and therapeutic treatment of Alzheimer's
     disease. Preferred agents including N-terminal fragments of AB and
     antibodies binding to the same.
    beta amyloid epitope chimeric protein antibody Alzheimer disease
ST
    Antibodies and Immunoglobulins
TΤ
    RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (IgG1; β-amyloid epitopes, chimeric polypeptides and anti-Aβ
        antibodies for diagnosis and passive immunization treatment of
       Alzheimer's disease)
IT
    Antibodies and Immunoglobulins
    RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (IgG2; β-amyloid epitopes, chimeric polypeptides and anti-Aβ
        antibodies for diagnosis and passive immunization treatment of
       Alzheimer's disease)
IT
    Antibodies and Immunoglobulins
    RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (IqG3; β-amyloid epitopes, chimeric polypeptides and anti-Aβ
        antibodies for diagnosis and passive immunization treatment of
       Alzheimer's disease)
IT
    Antibodies and Immunoglobulins
    RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (IqG4; β-amyloid epitopes, chimeric polypeptides and anti-Aβ
        antibodies for diagnosis and passive immunization treatment of
       Alzheimer's disease)
IT
    Antibodies and Immunoglobulins
     RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (IgG; β-amyloid epitopes, chimeric polypeptides and anti-Aβ
        antibodies for diagnosis and passive immunization treatment of
       Alzheimer's disease)
IT
     Immunostimulants
        (adjuvants, Freund's incomplete; β-amyloid epitopes, chimeric
       polypeptides and anti-Aß antibodies for diagnosis and passive
        immunization treatment of Alzheimer's disease)
IT
     Immunostimulants
        (adjuvants; β-amyloid epitopes, chimeric polypeptides and
        anti-AB antibodies for diagnosis and passive immunization
        treatment of Alzheimer's disease)
IT
    Drug delivery systems
        (carriers; β-amyloid epitopes, chimeric polypeptides and
        anti-Aß antibodies for diagnosis and passive immunization
        treatment of Alzheimer's disease)
    Antibodies and Immunoglobulins
TT
    RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
    DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (chimeric; \(\beta\)-amyloid epitopes, chimeric polypeptides and
       anti-Aß antibodies for diagnosis and passive immunization
       treatment of Alzheimer's disease)
IT
    Mental disorder
        (cognitive; β-amyloid epitopes, chimeric polypeptides and
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anti-Aß antibodies for diagnosis and passive immunization treatment of Alzheimer's disease) Cognition IT(disorder;  $\beta$ -amyloid epitopes, chimeric polypeptides and anti-Aß antibodies for diagnosis and passive immunization treatment of Alzheimer's disease) Antibodies and Immunoglobulins TΤ RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (fragments;  $\beta$ -amyloid epitopes, chimeric polypeptides and anti-Aß antibodies for diagnosis and passive immunization treatment of Alzheimer's disease) Antibodies and Immunoglobulins TT RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (heavy chain; β-amyloid epitopes, chimeric polypeptides and anti-Aß antibodies for diagnosis and passive immunization treatment of Alzheimer's disease) Antibodies and Immunoglobulins IT RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (humanized; β-amyloid epitopes, chimeric polypeptides and anti-Aß antibodies for diagnosis and passive immunization treatment of Alzheimer's disease) TΤ Diagnosis (immunodiagnosis; β-amyloid epitopes, chimeric polypeptides and anti-Aß antibodies for diagnosis and passive immunization treatment of Alzheimer's disease) TTDrug delivery systems (injections, i.m.; β-amyloid epitopes, chimeric polypeptides and anti-Aß antibodies for diagnosis and passive immunization treatment of Alzheimer's disease) ITDrug delivery systems (injections, i.p.; β-amyloid epitopes, chimeric polypeptides and anti-Aß antibodies for diagnosis and passive immunization treatment of Alzheimer's disease) IT Drug delivery systems (injections, i.v.; β-amyloid epitopes, chimeric polypeptides and anti-Aß antibodies for diagnosis and passive immunization treatment of Alzheimer's disease) IT Drug delivery systems (injections, s.c.;  $\beta$ -amyloid epitopes, chimeric polypeptides and anti-Aß antibodies for diagnosis and passive immunization treatment of Alzheimer's disease) IT Antibodies and Immunoglobulins RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (light chain;  $\beta$ -amyloid epitopes, chimeric polypeptides and anti-Aß antibodies for diagnosis and passive immunization treatment of Alzheimer's disease) IT Epitopes (mapping; β-amyloid epitopes, chimeric polypeptides and anti-Aß antibodies for diagnosis and passive immunization treatment of Alzheimer's disease) Antibodies and Immunoglobulins IT RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(monoclonal; β-amyloid epitopes, chimeric polypeptides and

anti-A $\beta$  antibodies for diagnosis and passive immunization treatment of Alzheimer's disease) IT Lipid A RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  $(monophosphates; \beta-amyloid epitopes, chimeric polypeptides and$ anti-Aß antibodies for diagnosis and passive immunization treatment of Alzheimer's disease) Drug delivery systems IT (nasal; β-amyloid epitopes, chimeric polypeptides and anti-Aβ antibodies for diagnosis and passive immunization treatment of Alzheimer's disease) Drug delivery systems TT (oral; β-amyloid epitopes, chimeric polypeptides and anti-Aβ antibodies for diagnosis and passive immunization treatment of Alzheimer's disease) Antibodies and Immunoglobulins IT RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (polyclonal;  $\beta$ -amyloid epitopes, chimeric polypeptides and anti-Aß antibodies for diagnosis and passive immunization treatment of Alzheimer's disease) Drug delivery systems TΤ (topical; β-amyloid epitopes, chimeric polypeptides and anti-Aß antibodies for diagnosis and passive immunization treatment of Alzheimer's disease) TT Amyloid RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  $(\beta$ -;  $\beta$ -amyloid epitopes, chimeric polypeptides and anti-Aß antibodies for diagnosis and passive immunization treatment of Alzheimer's disease) TΤ Adoptive immunotherapy Alzheimer's disease Amyloidosis B cell (lymphocyte) Blood Down's syndrome Epitopes Human Phagocytosis Protein sequences Susceptibility (genetic) Test kits  $(\beta$ -amyloid epitopes, chimeric polypeptides and anti-A $\beta$ antibodies for diagnosis and passive immunization treatment of Alzheimer's disease) IT Amyloid precursor proteins RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (β-amyloid epitopes, chimeric polypeptides and anti-Aβ antibodies for diagnosis and passive immunization treatment of Alzheimer's disease) Antibodies and Immunoglobulins RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (β-amyloid epitopes, chimeric polypeptides and anti-Aβ antibodies for diagnosis and passive immunization treatment of

Alzheimer's disease)

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Immunoglobulin receptors
IT
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (β-amyloid epitopes, chimeric polypeptides and anti-Aβ
        antibodies for diagnosis and passive immunization treatment of
        Alzheimer's disease)
                   721871-28-9
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IT
     721870-93-5
     RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP
     (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (amino acid sequence; β-amyloid epitopes, chimeric polypeptides
        and anti-Aß antibodies for diagnosis and passive immunization
        treatment of Alzheimer's disease)
IT
     721871-40-5
     RL: PRP (Properties)
        (unclaimed protein sequence; amyloid β epitopes, chimeric
        polypeptides and anti-Aß antibodies for diagnosis and passive
        immunization treatment of Alzheimer's disease)
IT
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     RL: PRP (Properties)
        (unclaimed sequence; amyloid β epitopes, chimeric polypeptides and
        anti-Aß antibodies for diagnosis and passive immunization
        treatment of Alzheimer's disease)
IT
     107761-42-2, Human \beta-amyloid peptide-(1-42)
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     (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (β-amyloid epitopes, chimeric polypeptides and anti-Aβ
        antibodies for diagnosis and passive immunization treatment of
        Alzheimer's disease)
IT
     7784-30-7, Aluminum phosphate
                                     21645-51-2, Aluminum hydroxide, biological
               141256-04-4, QS 21
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     (Biological study); USES (Uses)
        (β-amyloid epitopes, chimeric polypeptides and anti-Aβ
        antibodies for diagnosis and passive immunization treatment of
        Alzheimer's disease)
RE.CNT
        393
              THERE ARE 393 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Aguzzi; Nature 1997, V389, P795 HCAPLUS
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(3) Akiyama; Neurobiology of Aging 2000, V21, P383 HCAPLUS
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- (22) Anon; WO 9302189 1993 HCAPLUS
- (23) Anon; WO 9314200 1993 HCAPLUS
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## IT 176390-00-4

RL: PRP (Properties)

(unclaimed sequence; amyloid  $\beta$  epitopes, chimeric polypeptides and anti-A $\beta$  antibodies for diagnosis and passive immunization treatment of Alzheimer's disease)

RN 176390-00-4 HCAPLUS

CN L-Phenylalanine, L- $\alpha$ -glutamyl-L-valyl-L-histidyl-L-glutaminyl-L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-B

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TI Stereoselective Interactions of Peptide Inhibitors with the  $\beta$ -Amyloid Peptide

AU Chalifour, Robert J.; McLaughlin, Richard W.; Lavoie, Louis; Morissette, Celine; Tremblay, Nadine; Boule, Marie; Sarazin, Philippe; Stea, Dino; Lacombe, Diane; Tremblay, Patrick; Gervais, Francine

CS Neurochem Inc., Saint-Laurent, QC, H4S 2A1, Can.

SO Journal of Biological Chemistry (2003), 278(37), 34874-34881 CODEN: JBCHA3; ISSN: 0021-9258

PB American Society for Biochemistry and Molecular Biology

DT Journal

LA English

CC 1-3 (Pharmacology)

AB Residues 16-20 of the  $\beta$ -amyloid peptide (A $\beta$ ) function as a self-recognition element during Aß assembly into fibers. Peptides containing this motif retain the ability to interact with AB and, in some cases, potently inhibit its assembly. Replacing L- with D-amino acids could stabilize such peptides and permit their evaluation as therapeutic agents for Alzheimer's disease. Here we have assessed the effect that such a chiral reversal has on inhibitory potency. D-enantiomers of five peptides, KLVFFA, KKLVFFA, KFVFFA, KIVFFA, and KVVFFA, were unexpectedly more active as inhibitors in an in vitro fibrillogenesis assay. CD showed that D-KLVFFA more effectively prevented A $\beta$  adopting the  $\beta$ -sheet secondary structure correlated with fibrillogenesis. Electron microscopy showed that fiber formation was also more strongly inhibited by D-KLVFFA. Heterochiral inhibition was confirmed using D-AB, on the principle that enantiomeric proteins exhibit reciprocal chiral biochem. interactions. With D-Aß, L-KLVFFA was the more potent inhibitor, rather than D-KLVFFA. Most significantly, D-peptides were more potent at reducing the toxicity of both Aβ1-40 and Aβ1-42 toward neuronal cells in culture. This unforeseen heterochiral stereoselectivity of Aβ for D-peptide inhibitors should be considered during future design of peptide-based inhibitors of AB neurotoxicity and fibrillogenesis. stereoselective interaction peptide inhibitor beta amyloid peptide;

ST stereoselective interaction peptide inhibitor beta amyloid peptide; Alzheimers disease treatment peptide

IT Organelle

(fibril, inhibition of fibrillogenesis; stereoselective interactions of

peptide inhibitors with the  $\beta$ -amyloid peptide in relation to Alzheimer's disease treatment) Self-assembly IT (inhibition of  $A\beta$  assembly; stereoselective interactions of peptide inhibitors with the  $\beta$ -amyloid peptide in relation to Alzheimer's disease treatment) Conformational transition IT **B-Sheet** (inhibition of A $\beta$  transition to  $\beta$ -sheet secondary structure; stereoselective interactions of peptide inhibitors with the β-amyloid peptide in relation to Alzheimer's disease treatment) IT Cytoprotective agents (neuroprotective, protection against neurotoxicity of Aβ; stereoselective interactions of peptide inhibitors with the  $\beta$ -amyloid peptide in relation to Alzheimer's disease treatment) TT Nerve Neurotoxicity (protection against neurotoxicity of AB; stereoselective interactions of peptide inhibitors with the β-amyloid peptide in relation to Alzheimer's disease treatment) IT Alzheimer's disease Anti-Alzheimer's agents Human Structure-activity relationship (stereoselective interactions of peptide inhibitors with the β-amyloid peptide in relation to Alzheimer's disease treatment) IT(toxicity, protection against neurotoxicity of Aβ; stereoselective interactions of peptide inhibitors with the  $\beta$ -amyloid peptide in relation to Alzheimer's disease treatment) IT RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study) (β-; stereoselective interactions of peptide inhibitors with the  $\beta$ -amyloid peptide in relation to Alzheimer's disease treatment) IT9005-49-6, Heparin, biological studies RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibition of heparin-promoted Aß fibrillogenesis; stereoselective interactions of peptide inhibitors with the β-amyloid peptide in relation to Alzheimer's disease treatment) IT107761-42-2, Amyloid β 1-42 131438-79-4, Amyloid  $\beta$ peptide(1-40) (synthetic) RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study) (stereoselective interactions of peptide inhibitors with the β-amyloid peptide in relation to Alzheimer's disease treatment) IT190775-14-5 206198-57-4 307299-71-4 307299-72-5 307299-75-8 342877-55-8 342877-57-0 342877-58-1 342877-59-2 342877-64-9 RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (stereoselective interactions of peptide inhibitors with the β-amyloid peptide in relation to Alzheimer's disease treatment) RE.CNT THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD RE (1) Atwood, C; J Neurochem 2000, V75, P1219 HCAPLUS (2) Colon, W; Methods Enzymol 1999, V309, P605 HCAPLUS (3) Corigliano-Murphy, M; Int J Pept Protein Res 1985, V25, P225 HCAPLUS (4) Esler, W; Biochemistry 1996, V35, P13914 HCAPLUS (5) Esler, W; Biopolymers 1999, V49, P505 HCAPLUS (6) Feifel, B; J Biol Chem 1998, V273, P11999 HCAPLUS (7) Findeis, M; Biochemistry 1999, V38, P6791 HCAPLUS

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- IT 190775-14-5

RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(stereoselective interactions of peptide inhibitors with the

β-amyloid peptide in relation to Alzheimer's disease treatment)

RN 190775-14-5 HCAPLUS

CN L-Alanine, L-lysyl-L-lysyl-L-leucyl-L-valyl-L-phenylalanyl-L-phenylalanyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-B

-NH<sub>2</sub>

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L45 ANSWER 3 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
AN
    2002:770145 HCAPLUS
DN
    137:284351
ED
    Entered STN: 10 Oct 2002
TI
    Peptides and pharmaceutical compositions thereof for treatment of
    disorders or diseases associated with abnormal protein folding into
    amyloid or amyloid-like deposits
IN
    Soto-Jara, Claudio; Baumann, Marc H.; Frangione, Blas
    New York University, USA
PA
    U.S., 51 pp., Cont.-in-part of U.S. 5,948,763.
SO
    CODEN: USXXAM
DT
    Patent
LΑ
    English
    ICM A61K038-00
TC
    ICS C07K016-00
NCL 530326000
    63-6 (Pharmaceuticals)
    Section cross-reference(s): 1
FAN.CNT 3
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                       B1 20021008 US 1996-766596 19961212 <--
A 19990907 US 1996-630645 19960410 <--
A1 20030508 US 2002-235483 20020906 <--
    US 6462171
    US 5948763
                                                              20020906 <--
    US 2003087407
                       B2 19950607 <--
PRAI US 1995-478326
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                       A2 19960410 <--
                       A1 19961212 <--
    US 1996-766596
CLASS
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              CLASS PATENT FAMILY CLASSIFICATION CODES
 US 6462171
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               ICS
                      C07K016-00
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                      530326000
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                      A61K049/00H6; C07K005/08H2A; C07K014/47A3; G01N033/68V2
 US 5948763
                ECLA
                      A61K049/00H6; C07K005/08H2A; C07K014/47A3; G01N033/68V2
 US 2003087407
                      A61K049/00H6; C07K005/08H2A; C07K014/47A3; G01N033/68V2
                ECLA
                                                                        <--
    Novel peptides capable of interacting with a hydrophobic \beta-sheet
ΔR
    or amyloid-like deposit formation inhibit and structurally block the
     abnormal folding of proteins and peptides into amyloid or amyloid-like
```

forming cluster of amino acid residues on a protein or peptide for amyloid deposits and into pathol.  $\beta$ -sheet-rich conformation as precursors thereof. Methods for preventing, treating or detecting disorders or diseases associated with amyloid-like fibril deposits, such as Alzheimer's disease and prion-related encephalopathies, are also provided.

```
peptide protein folding inhibitor amyloid prion disease
ST
ΙT
     Drug delivery systems
        (carriers; peptides and pharmaceutical compns. thereof for treatment of
        disorders or diseases associated with abnormal protein folding into
        amyloid or amyloid-like deposits)
IT
     Prion diseases
     Protein folding
     Protein sequences
        (peptides and pharmaceutical compns. thereof for treatment of disorders
        or diseases associated with abnormal protein folding into amyloid or
        amyloid-like deposits)
IT
     Amyloid
     RL: ADV (Adverse effect, including toxicity); BSU (Biological study,
     unclassified); BIOL (Biological study)
        (peptides and pharmaceutical compns. thereof for treatment of disorders
        or diseases associated with abnormal protein folding into amyloid or
        amyloid-like deposits)
IT
     Amyloid
     RL: ADV (Adverse effect, including toxicity); BSU (Biological study,
     unclassified); BIOL (Biological study)
        (β-; peptides and pharmaceutical compns. thereof for treatment of
        disorders or diseases associated with abnormal protein folding into
        amyloid or amyloid-like deposits)
     Amino acids, biological studies
IT
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (D-; peptides and pharmaceutical compns. thereof for treatment of
        disorders or diseases associated with abnormal protein folding into
        amyloid or amyloid-like deposits)
TΤ
     112805-81-9
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                                               162471-00-3
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                                182912-70-5
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                                                             182912-74-9
     182912-76-1
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                                 464892-88-4
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     RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic
     use); BIOL (Biological study); USES (Uses)
        (peptides and pharmaceutical compns. thereof for treatment of disorders
        or diseases associated with abnormal protein folding into amyloid or
        amyloid-like deposits)
IT
     152286-31-2
                  173692-60-9
                                               467233-48-3
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     RL: PRP (Properties)
        (unclaimed sequence; peptides and pharmaceutical compns. thereof for
        treatment of disorders or diseases associated with abnormal protein
        folding into amyloid or amyloid-like deposits)
RE.CNT
              THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Anderson; US 5169933 A 1992 HCAPLUS
(2) Anon; EP 359347 1990 HCAPLUS
(3) Anon; EP 0584452 1994 HCAPLUS
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#### TТ 464892-78-2

RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(peptides and pharmaceutical compns. thereof for treatment of disorders or diseases associated with abnormal protein folding into amyloid or amyloid-like deposits)

464892-78-2 HCAPLUS RN

L-Phenylalanine, L-lysyl-L-prolyl-L-valyl-L-phenylalanyl- (9CI) CN(CA INDEX NAME)

## Absolute stereochemistry.

- L45 ANSWER 4 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
- 2002:540135 HCAPLUS AΝ
- DN 137:108295
- ED Entered STN: 19 Jul 2002
- Vaccines comprising all-D fibril peptides for prevention and treatment of ΤI Alzheimer's and amyloid-related diseases
- IN Chalifour, Robert; Hebert, Lise; Kong, Xianqi; Gervais, Francine
- PA
- U.S. Pat. Appl. Publ., 28 pp., Cont.-in-part of U.S. Ser. No. 724,842. SO CODEN: USXXCO
- DT Patent
- English LΑ
- IC ICM A61K039-00
- NCL 424185100
- 15-2 (Immunochemistry)

# FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002094335	A1	20020718	US 2001-867847	20010529
	WO 2002096937	A2	20021205	WO 2002-CA763	20020529
	WO 2002096937	A3	20030710		
	W: AE. AG.	AL, AM, AT	L. AU. AZ.	BA. BB. BG. BR. BY. B	Z. CA. CH. CN.

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

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LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
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            UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
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                                                                  20020529
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PRAI US 1999-168594P
                        P
                               19991129
                         A2
    US 2000-724842
                               20001128
    US 2001-867847
                        Α
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    WO 2002-CA763
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CLASS
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US 2002094335 ICM
                       A61K039-00
                NCL
                       424185100
US 2002094335
                ECLA
                       A61K039/00D3; C07K014/47A3; C07K016/18
    The present invention relates to a stereochem. based "non-self" antigen
    vaccine for the prevention and/or treatment of Alzheimer's and other
    amyloid related diseases. The present invention provides a vaccine for
    the prevention and treatment of Alzheimer's and other amyloid related
    diseases, which overcomes the drawbacks associated with using naturally
    occurring peptides, proteins or immunogens. The vaccine comprises fibril
    peptides consisting of all- D-amino acids.
    D amino acid fibril peptide amyloid related disease; Alzheimer disease
    vaccine nonself fibril peptide
TΤ
    Gene, animal
    RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (APP; vaccines comprising all-D fibril peptides for prevention and
        treatment of Alzheimer's and amyloid-related diseases)
IT
    Brain, disease
    Prion diseases
        (Creutzfeldt-Jakob; vaccines comprising all-D fibril peptides for
       prevention and treatment of Alzheimer's and amyloid-related diseases)
TT
    Proteins
    RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (SAA (serum amyloid A), serum; vaccines comprising all-D fibril
       peptides for prevention and treatment of Alzheimer's and
       amyloid-related diseases)
IT
     Functional groups
        (acid; vaccines comprising all-D fibril peptides for prevention and
        treatment of Alzheimer's and amyloid-related diseases)
IT
    Macrophage
        (adherence region; vaccines comprising all-D fibril peptides for
       prevention and treatment of Alzheimer's and amyloid-related diseases)
IT
    Functional groups
        (alkoxy groups; vaccines comprising all-D fibril peptides for
       prevention and treatment of Alzheimer's and amyloid-related diseases)
IT
    Functional groups
        (alkoxycarbonyl groups; vaccines comprising all-D fibril peptides for
       prevention and treatment of Alzheimer's and amyloid-related diseases)
IT
    Functional groups
        (alkoxyphosphonyl; vaccines comprising all-D fibril peptides for
       prevention and treatment of Alzheimer's and amyloid-related diseases)
IT
    Functional groups
        (alkyloxysulfonyl; vaccines comprising all-D fibril peptides for
       prevention and treatment of Alzheimer's and amyloid-related diseases)
IT
    Brain, disease
```

(amyloid angiopathy; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) Functional groups IT (aryloxycarbonyl; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) TT Functional groups (aryloxyl; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) IT Functional groups (carbamyl; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) IT Toxicity (cellular; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) IT Infection Inflammation (chronic; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) Proteins IT RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (conjugates; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) ITNervous system, disease (degeneration; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) IT Amyloidosis (familial Mediterranean fever; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) IT Fever and Hyperthermia (familial Mediterranean; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) IT Organelle (fibril, formation inhibition; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) IT Proteins RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (fibril; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) Antibodies and Immunoglobulins ITRL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (heavy chain; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) ITDialysis (hemodialysis; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) IT Functional groups (hydroxycarbonyl; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) IT Antibodies and Immunoglobulins RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (light chain; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) IT Functional groups (lower alkyl; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT

Brain, disease Prion diseases

(mad cow; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) Diabetes mellitus TТ (non-insulin-dependent; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) TТ Antigens RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (non-self; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) TТ Hormones, animal, biological studies RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (peptide; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) ΙT Salts, biological studies RL: BSU (Biological study, unclassified); BIOL (Biological study) (pharmaceutical acceptable; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) Esters, biological studies IT RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (pharmaceutical acceptable; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) ŤΨ Functional groups (phosphono; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) IT Proteins RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (precursor, fibril; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) TT Prion proteins RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (precursor; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) Brain, disease TT Prion diseases (scrapie; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) ITMutagenesis (site-directed, deletion; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) TТ (site-directed, insertion; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) IT(site-directed, substitution; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) IT Functional groups (sulfo group; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) IT Acyl groups Alzheimer's disease Amino group Amyloidosis

Drug delivery systems

Epitopes

IT

IT

IT

TT

TΥ

IT

TΤ

TT

TΤ

IT

TT

Human Hydroxyl group Peptidomimetics Prion diseases Rheumatoid arthritis Tuberculosis Vaccines β-Sheet (vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) Antibodies and Immunoglobulins RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) Amyloid precursor proteins RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) Aromatic compounds RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) Gelsolin RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) Heterocyclic compounds RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) Keratins RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) Transthyretin RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) Fibrinogens RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (α chain; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) Microglobulins RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (β-microglobulins; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) Amino acids, biological studies RL: BSU (Biological study, unclassified); BIOL (Biological study) (D-; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases) 165196-29-2 342877-52-5 342877-53-6 342877-54-7 342877-55-8 342877-56-9 **342877-57-0 342877-58-1** 342877-59-2 342877-60-5 **342877-61-6** 342877-62-7 342877-63-8 342877-64-9

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342877-65-0 342877-66-1 342877-67-2
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     RL: BSU (Biological study, unclassified); PRP (Properties); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (vaccines comprising all-D fibril peptides for prevention and treatment
        of Alzheimer's and amyloid-related diseases)
IT
     9001-63-2, Lysozyme
                           85637-73-6, Atrial natriuretic peptide
                                                                      91448-99-6,
     Cystatin C
                  106602-62-4, Islet amyloid polypeptide
                                                            216864-07-2D,
     \alpha-Synuclein, derivs.
                            216864-08-3D, \beta-Synuclein, derivs.
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (vaccines comprising all-D fibril peptides for prevention and treatment
        of Alzheimer's and amyloid-related diseases)
ТТ
     342877-55-8
     RL: BSU (Biological study, unclassified); PRP (Properties); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (vaccines comprising all-D fibril peptides for prevention and treatment
        of Alzheimer's and amyloid-related diseases)
RN
     342877-55-8 HCAPLUS
     D-Alanine, D-lysyl-D-leucyl-D-valyl-D-phenylalanyl-D-phenylalanyl- (9CI)
CN
     (CA INDEX NAME)
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Absolute stereochemistry.

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ANSWER 5 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
L45
     2002:89879 HCAPLUS
AN
DN
     136:139864
     Entered STN: 01 Feb 2002
ED
TI
     Amyloid targeting imaging agents
IN
     Gervais, Francine; Kong, Xianqi; Chalifour, Robert;
     Migneault, David
PA
     Neurochem, Inc., Can.
SO
     PCT Int. Appl., 57 pp.
     CODEN: PIXXD2
DT
     Patent
     English
LA
IC
     ICM A61K051-04
     ICS A61K051-08
CC
     63-6 (Pharmaceuticals)
     Section cross-reference(s): 8
FAN.CNT 2
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                              20020131 WO 2001-CA1071
PΙ
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    WO 2002007781
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            LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
            RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
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                             20020822 US 2001-915092
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                              20020131 CA 2001-2416617
20030423 EP 2001-956226
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CLASS
             CLASS PATENT FAMILY CLASSIFICATION CODES
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WO 2002007781 ICM
                      A61K051-04
                      A61K051-08
               ICS
US 2002115717 ECLA
                      A61K051/04Z; A61K051/08Z
os
    MARPAT 136:139864
    Amyloid-targeting imaging agents such as radiolabeled amyloid targeting
AB
    mols. and amyloid targeting mol.-chelator conjugates for imaging, e.g.,
     amyloid plagues in vivo, and/or for the treatment of amyloidosis disorders
     are described. The invention provides amyloid-targeting imaging agents
     that are useful for imaging sites of amyloid disease. The imaging agents
     are capable of binding specifically to amyloid plaques, as an aid in
     diagnosis and/or early treatment of amyloidosis disorders.
     amyloid targeting imaging agent; amyloidosis imaging agent; peptide
ST
     radionuclide complex imaging agent
IT
     Brain, disease
     Prion diseases
        (Creutzfeldt-Jakob; amyloid targeting imaging agents)
ΙT
     Imaging
        (acoustic; amyloid targeting imaging agents)
     Brain, disease
IT
        (amyloid angiopathy; amyloid targeting imaging agents)
IT
     Alzheimer's disease
    Amyloidosis
     Buffers
     Diagnosis
     Imaging agents
     Radiopharmaceuticals
     Reducing agents
        (amyloid targeting imaging agents)
TТ
     Amyloid
     RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
        (amyloid targeting imaging agents)
IT
     Chelates
     RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study);
     USES (Uses)
        (amyloid targeting imaging agents)
     Radionuclides, biological studies
IT
     RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study);
     USES (Uses)
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(imaging agents labeled with; amyloid targeting imaging agents) IΤ Brain, disease Prion diseases (kuru; amyloid targeting imaging agents) Brain, disease IT Prion diseases (mad cow; amyloid targeting imaging agents) IT Diabetes mellitus (non-insulin-dependent; amyloid targeting imaging agents) ΙT Peptides, biological studies RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (radiolabeled conjugates; amyloid targeting imaging agents) IT Brain, disease Prion diseases (scrapie; amyloid targeting imaging agents) 100-88-9D, Cyclohexylsulfamic acid, radiolabeled conjugates IT 573-58-0D. Congo red, radiolabeled conjugates 959-81-9D, radiolabeled conjugates 1119-23-9D, radiolabeled conjugates 1119-25-1D, radiolabeled conjugates 1119-71-7D, radiolabeled conjugates 1119-93-3D, radiolabeled conjugates 1119-95-5D, radiolabeled conjugates 1119-96-6D, radiolabeled conjugates 1119-98-8D, radiolabeled conjugates 1119-99-9D, radiolabeled conjugates 1120-00-9D, radiolabeled conjugates 1120-03-2D, radiolabeled conjugates 1120-05-4D, radiolabeled conjugates 1138-84-7D, radiolabeled conjugates 1829-00-1D, Thiazol yellow g, radiolabeled conjugates 2390-54-7D, Thioflavin t, radiolabeled conjugates 2610-05-1D, Chicago sky blue 6B, radiolabeled conjugates 2785-06-0D, radiolabeled conjugates 3095-95-2D, radiolabeled conjugates 3119-93-5D, radiolabeled conjugates 4033-31-2D, radiolabeled conjugates 3785-01-1D, radiolabeled conjugates 4443-32-7D, radiolabeled conjugates 4444-23-9D, radiolabeled conjugates 4481-44-1D, radiolabeled conjugates 4720-61-0D, radiolabeled conjugates 10043-49-9D, Au 198, imaging agents labeled with 10043-66-0D, I 131, 10098-91-6D, Y 90, imaging agents labeled imaging agents labeled with with 10098-97-2D, Sr 90, imaging agents labeled with 10198-40-0D, Co 60, imaging agents labeled with 13501-35-4D, radiolabeled conjugates 13967-65-2D, Ho 166, imaging agents labeled with 13981-25-4D, imaging agents labeled with 13981-50-5D, Co 57, imaging agents labeled with 13981-56-1D, Fluorine 18, imaging agents labeled with 14119-09-6D, Ga 67, imaging agents labeled with 14158-27-1D, Sr 89, imaging agents labeled with 14158-31-7D, I 125, imaging agents labeled with 14276-65-4D, Gd-153, imaging agents labeled with 14378-26-8D, Rhenium-188, imaging agents labeled with 14391-11-8D, Au 199, imaging agents labeled with 14392-02-0D, Cr 51, imaging agents labeled with 14913-89-4D, Rh 105, imaging agents labeled with 14933-09-6D, radiolabeled conjugates 14981-64-7D, imaging agents labeled with 14998-63-1D, Rhenium-186, imaging agents labeled with 15064-65-0D, Tl 201, imaging agents labeled with 15214-89-8D, radiolabeled conjugates 15715-08-9D, I 123, imaging agents labeled with 15750-15-9D, imaging agents labeled with 15757-86-5D, Copper-67, imaging agents labeled with 15758-35-7D, imaging agents labeled with 15766-00-4D, Sm 153, imaging agents labeled with 20694-16-0 29777-99-9D, radiolabeled conjugates 38878-02-3D, radiolabeled conjugates 40265-71-2D, radiolabeled 42457-53-4D, radiolabeled conjugates 42846-15-1D, radiolabeled conjugates 49625-94-7D, radiolabeled conjugates 50567-35-6D, radiolabeled conjugates 52962-42-2D, radiolabeled 58431-88-2D, radiolabeled conjugates conjugates 63555-51-1D, radiolabeled conjugates 63585-09-1D, radiolabeled conjugates 72943-20-5D, radiolabeled conjugates 75708-92-8D, Folic acid dihydrate, 76936-63-5D, radiolabeled conjugates radiolabeled conjugates 77337-76-9D, radiolabeled conjugates 80969-51-3D, radiolabeled 82611-83-4D, radiolabeled conjugates conjugates 83678-67-5, 92014-92-1D, radiolabeled conjugates Gadolinium-DOTA 101373-15-3D,

radiolabeled conjugates 153247-40-6D, radiolabeled conjugates

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176390-19-5D, radiolabeled conjugates
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conjugates 183746-61-4D, radiolabeled conjugates
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conjugates
radiolabeled conjugates
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conjugates
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radiolabeled conjugates
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conjugates
RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study);
USES (Uses)
   (amyloid targeting imaging agents)
14133-76-7D, imaging agents labeled with
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labeled with
RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study);
USES (Uses)
   (metastable; amyloid targeting imaging agents)
153247-40-6D, radiolabeled conjugates
RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study);
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TT

IT

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USES (Uses)

(amyloid targeting imaging agents)

RN 153247-40-6 HCAPLUS

L-Phenylalanine, L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX CN NAME)

Absolute stereochemistry.

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L45
    ANSWER 6 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
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AN 2001:844884 HCAPLUS

DN 136:665

ED Entered STN: 21 Nov 2001

ТT Modified peptide modulators of amyloid aggregation

IMFinders, Mark A.; Benjamin, Howard; Garnick, Marc B.; Gefter, Malcolm L.; Hundal, Arvind; Kasman, Laura; Musso, Gary; Signer, Ethan R.; Wakefield, James; Reed, Michael J.

PΑ Praecis Pharmaceuticals Incorporated, USA

SO U.S., 54 pp., Cont.-in-part of U.S. Ser. No. 548,998, abandoned. CODEN: USXXAM

DTPatent

LA English

ICM A61K038-02 IC

ICS A61K038-17; C07K001-113; C07K014-47

NCL 424094300

CC 1-11 (Pharmacology)

Section cross-reference(s): 9, 34, 63

NCL

**ECLA** 

424094300

C07K014/47A3

US 6319498

FAN.CNT 7		, , , , , , ,			
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI US 6319498	B1	20011120	US 1996-617267	19960314 <	
US 5817626	A	19981006	US 1995-404831	19950314 <	
US 5854215	A	19981229	US 1995-475579	19950607 <	
AU 759036	B2	20030403	AU 2000-35389	20000519 <	
US 2002098173	A1	20020725	US 2001-972475	20011004 <	
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US 1995-548998	B2	19951027	<		
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US 1996-617267	A1	19960314	<		
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US 2001-972475	A1	20011004			
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ICS	A61K038-17; C07K001-113; C07K014-47				

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                        C07K014/47A3
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     MARPAT 136:665
os
     Compds. that modulate the aggregation of amyloidogenic proteins or
AB
     peptides are disclosed. The modulators of the invention can promote
     amyloid aggregation or, more preferably, can inhibit natural amyloid
     aggregation. In a preferred embodiment, the compds. modulate the
     aggregation of natural \beta amyloid peptides (\beta-AP). In a
     preferred embodiment, the \beta amyloid modulator compds. are comprised
     of an AB aggregation core domain and a modifying group coupled
     thereto such that the compound alters the aggregation or inhibits the
     neurotoxicity of natural $\beta$ amyloid peptides when contacted with the
     peptides. Furthermore, the modulators are capable of altering natural
     \beta-AP aggregation when the natural \beta-APs are in a molar excess
     amount relative to the modulators. Pharmaceutical compns. comprising the
     compds. of the invention, and diagnostic and treatment methods for
     amyloidogenic diseases using the compds. of the invention, are also
     disclosed.
ST
     peptide deriv prepn amyloid aggregation modulation; amyloidogenic disease
     peptide deriv amyloid aggregation modulation
TΤ
     Amyloid
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (A, modified; modified peptide modulators of amyloid aggregation)
TΤ
     Apolipoproteins
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (A-I, modified; modified peptide modulators of amyloid aggregation)
TΤ
     Proteins
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (amyloidogenic, modified; modified peptide modulators of amyloid
        aggregation)
IT
     Antibodies and Immunoglobulins
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (light chain, \kappa and \lambda, modified; modified peptide
        modulators of amyloid aggregation)
TT
    Drug delivery systems
    Nerve
     Neurotoxicity
     Pharmacokinetics
        (modified peptide modulators of amyloid aggregation)
IT
     Amyloid
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (modified peptide modulators of amyloid aggregation)
IT
     Fibrinogens
     Gelsolin
     Peptides, biological studies
     Prion proteins
     Transthyretin
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (modified; modified peptide modulators of amyloid aggregation)
IT
     Peptides, biological studies
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (retro-inverso; modified peptide modulators of amyloid aggregation)
IT
    Nerve
        (toxicity; modified peptide modulators of amyloid aggregation)
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IT

Amyloid

```
RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (β-; modified peptide modulators of amyloid aggregation)
IT
     Microglobulins
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (β2-, modified; modified peptide modulators of amyloid
        aggregation)
IT
     Amino acids, biological studies
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (D-; modified peptide modulators of amyloid aggregation)
IT
     81-25-4, Cholic acid
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (modified peptide modulators of amyloid aggregation)
IT
     183745-81-5DP, biotinylated 350032-71-2DP, biotinylated
     RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic
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     (Preparation); USES (Uses)
        (modified peptide modulators of amyloid aggregation)
IT
     2577-40-4D, N-terminal cholyl derivs. 10183-34-3D, N-terminal cholyl
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               13116-21-7D, N-terminal cholyl derivs. 64533-15-9D, N-terminal
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IT
     9001-63-2D, Lysozyme, modified
                                     9007-12-9D, Calcitonin, modified
     56645-65-9D, Procalcitonin, modified 85637-73-6D, Atrial natriuretic
     factor, modified
                       91448-99-6D, Cystatin C, modified
                                                           106602-62-4D, Islet
     amyloid polypeptide, modified
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RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
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        (modified peptide modulators of amyloid aggregation)
IT
     183745-81-5D, resin-bound
     RL: PRP (Properties); RCT (Reactant); RACT (Reactant or reagent)
        (modified peptide modulators of amyloid aggregation)
     58-85-5, Biotin
TT
     RL: RCT (Reactant); RACT (Reactant or reagent)
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                   169593-16-2 365537-65-1 374068-23-2 375376-36-6
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- IT 134649-29-9D, N-terminal cholyl derivs.
  - RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (modified peptide modulators of amyloid aggregation)
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Absolute stereochemistry.

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PAGE 1-B

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L45 ANSWER 7 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
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AN 2001:757810 HCAPLUS

DN 135:298818

ED Entered STN: 17 Oct 2001

TI D-amino acid-containing peptide modulators of  $\beta\text{-amyloid}$  peptide aggregation

IN Findeis, Mark A.; Gefter, Malcolm L.; Musso, Gary; Signer, Ethan R.; Wakefield, James; Molineaux, Susan; Chin, Joseph; Lee, Jung-Ja; Kelley, Michael; Komar-Panicucci, Sonja; Arico-Muendel, Christopher C.; Phillips, Kathryn; Hayward, Neil J.

PA Praecis Pharmaceuticals, Inc., USA

SO U.S., 44 pp., Cont.-in-part of U.S. Ser. No. 616,081. CODEN: USXXAM

DT Patent

LA English

IC ICM A61K038-06 ICS A61K038-07; A61K038-08; A61K038-10

NCL 514002000

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WO 9808868 A1 19980305 WO 1997-US15166 19970827 <--
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AB
      Compds. that modulate natural \beta amyloid peptide aggregation are
      provided. The modulators of the invention comprise a peptide, preferably
      based on a \beta amyloid peptide, that is comprised entirely of D-amino
       acids. Preferably, the peptide comprises 3-5 D-amino acid residues and
       includes at least two D-amino acid residues independently selected from
       D-leucine, D-phenylalanine, and D-valine. In a particularly preferred
       embodiment, the peptide is a retro-inverso isomer of a \beta amyloid
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peptide, preferably a retro-inverso isomer of AB17-21 . In certain

embodiments, the peptide is modified at the amino-terminus, the carboxyl-terminus, or both. Preferred amino-terminal modifying groups include cyclic, heterocyclic, polycyclic and branched alkyl groups. Preferred carboxyl-terminal modifying groups include an amide group, an alkyl amide group, an aryl amide group, and a hydroxy group. Pharmaceutical compns. comprising the compds. of the invention, and diagnostic and treatment methods for amyloidogenic diseases (e.g. Alzheimer's disease) using the compds. of the invention, are also disclosed.

ST D amino acid peptide amyloid modulator; Alzheimer disease D amino acid peptide; retro inverso peptide amyloid modulator

IT Biological transport

(drug; D-amino acid-containing peptide modulators of  $\beta$ -amyloid peptide aggregation)

IT Cytoprotective agents

(neuroprotectants; D-amino acid-containing peptide modulators of  $\beta$ -amyloid peptide aggregation)

IT Toxicity

(neurotoxicity; D-amino acid-containing peptide modulators of  $\beta$ -amyloid peptide aggregation)

IT Cerebrospinal fluid

(peptide stability in; D-amino acid-containing peptide modulators of  $\beta$ -amyloid peptide aggregation)

IT Peptides, biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(retro-inverso; D-amino acid-containing peptide modulators of  $\beta$ -amyloid peptide aggregation)

IT Nerve

(toxicity; D-amino acid-containing peptide modulators of  $\beta$ -amyloid peptide aggregation)

IT Amyloid

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

 $(\beta\text{--};\ D\text{-amino}\ acid\text{-containing}\ peptide\ modulators\ of\ \beta\text{-amyloid}\ peptide\ aggregation)$ 

IT Aggregation

 $(\beta\mbox{-amyloid peptide};\mbox{ $D$-amino acid-containing peptide modulators of }\beta\mbox{-amyloid peptide aggregation})$ 

IT Amino acids, biological studies

RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)

(D-; D-amino acid-containing peptide modulators of  $\beta\text{-amyloid}$  peptide aggregation)

IT Drug delivery systems

Pharmacokinetics

(D-amino acid-containing peptide modulators of  $\beta\text{-amyloid}$  peptide aggregation)

IT Peptides, biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(D-amino acid-containing peptide modulators of  $\beta$ -amyloid peptide aggregation)

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365538-53-0P 365538-54-1P 365538-55-2P 365538-56-3P RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(D-amino acid-containing peptide modulators of  $\beta$ -amyloid peptide aggregation)

IT

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365536-68-1

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RL: BAC (Biological activity or effector, except adverse); BSU (Biological
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derivative

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365536-66-9

365536-67-0

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RL: BAC (Biological activity or effector, except adverse); BSU (Biological
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   (D-amino acid-containing peptide modulators of \beta-amyloid peptide
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amino-terminal modified derivs. 365538-14-3D, modifying group derivs. 365538-17-6D, modifying group derivs. 365538-20-1D, modifying group 365538-23-4D, modifying group derivs. derivs. 365538-28-9D, modifying group derivs. 365538-31-4D, modifying group derivs. 365538-34-7D, 365538-37-0D, modifying group derivs. modifying group derivs. 365538-38-1D, modifying group derivs. 365538-39-2D, modifying group 365538-40-5D, modifying group derivs. derivs. 365538-41-6 365538-42-7 365538-43-8 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (D-amino acid-containing peptide modulators of  $\beta$ -amyloid peptide aggregation) 176390-05-9 176390-09-3 182912-78-3 176390-18-4 206198-57-4 365537-51-5 365537-52-6 RL: PRP (Properties) (D-amino acid-containing peptide modulators of β-amyloid peptide aggregation) RE.CNT 79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS RECORD (1) Anon; EP 554887 A1 1993 HCAPLUS (2) Anon; WO 9304194 1993 HCAPLUS (3) Anon; WO 9428412 1994 HCAPLUS (4) Anon; EP 641861 Al 1995 HCAPLUS (5) Anon; EP 681844 Al 1995 HCAPLUS (6) Anon; WO 9505394 1995 HCAPLUS (7) Anon; WO 9505604 1995 HCAPLUS (8) Anon; WO 9507093 1995 HCAPLUS (9) Anon; WO 9508999 1995 HCAPLUS (10) Anon; WO 9512815 1995 HCAPLUS (11) Anon; WO 9520979 1995 HCAPLUS (12) Barrow; J Mol Biol 1992, V225, P1075 HCAPLUS (13) Barrow; Science 1991, V253, P179 HCAPLUS (14) Brown; Analytical Biochemistry 1994, V217, P139 HCAPLUS (15) Burdick; Journal of Biological Chemistry 1992, V267(1), P546 HCAPLUS (16) Chantry; FEBS 1992, V296(2), P123 HCAPLUS (17) Clements; Biochemical Society Transactions 1993, V22, P16S (18) Come; Proc Natl Acad Sci USA 1993, V90, P5959 HCAPLUS (19) Evans; Proc Natl Acad Sci USA 1995, V92, P763 HCAPLUS (20) Fabian; Biochemical and Biophysical Research Communications 1993, V191(1), P232 HCAPLUS (21) Fabian; Eur J Biochem 1994, V221, P959 HCAPLUS (22) Findeis; US 5817626 1998 HCAPLUS (23) Findeis; US 5854204 1998 HCAPLUS (24) Findeis; US 5854215 1998 HCAPLUS (25) Findeis; US 5985242 1999 HCAPLUS (26) Flood, J; Proc Natl Acad Sci USA 1994, V91, P380 HCAPLUS (27) Fraser; Biochemistry 1992, V31, P10716 HCAPLUS (28) Fraser; J Mol Biol 1994, V244, P64 HCAPLUS (29) Gorevic, P; Biochemical and Biophysical Research Communications 1987, V147(2), P854 HCAPLUS (30) Gowing; J Biol Chem 1994, V269(15), P10987 HCAPLUS (31) Griffiths; US 6120768 2000 HCAPLUS (32) Halverson; Biochemistry 1990, V29(11), P2639 HCAPLUS (33) Hansen; J Immunol Meth 1989, V119, P203 MEDLINE (34) Hardy; Science 1992, V256, P184 HCAPLUS (35) Hendrix; J Am Che Soc 1992, V114, P7930 HCAPLUS (36) Hilbich; Eur J Biochem 1991, V201, P61 HCAPLUS (37) Hilbich; J Mol Biol 1991, V218, P149 HCAPLUS (38) Hilibich; J Mol Biol 1992, V228, P460 (39) Inouye, H; 1993 HCAPLUS (40) Jarrett; Biochemistry 1993, V32(18), P4693 HCAPLUS

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- IT 153247-40-6D, stereoisomer
  - RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
    - (D-amino acid-containing peptide modulators of  $\beta$ -amyloid peptide aggregation)
- RN 153247-40-6 HCAPLUS
- CN L-Phenylalanine, L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

fluorides)

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L45
    ANSWER 8 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
     2001:526090 HCAPLUS
AN
DN
     135:92861
     Entered STN: 20 Jul 2001
ED
     Process for the preparation of N\alpha-2-(4-nitrophenylsulfonyl) ethoxycar
ΤI
     bonyl amino acid fluorides
     Kim, Hack-Joo; Chweh, Weonu; Kim, Young-Cheol
IN
PA
     Hyundai Pharmaceutical Ind. Co., Ltd., S. Korea
SO
     PCT Int. Appl., 23 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
IC
     ICM C07K005-00
CC
     34-3 (Amino Acids, Peptides, and Proteins)
FAN.CNT 1
     PATENT NO.
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                               DATE
                                           APPLICATION NO.
                                                                  DATE
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                         A1
                               20010719
                                           WO 1999-KR810
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            IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
            MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
            SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,
            AZ, BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
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            CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI WO 1999-KR810
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 PATENT NO.
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WO 2001051505
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                       C07K005-00
                ECLA
                       C07C317/18; C07K001/06A2; C07K001/08D
os
     CASREACT 135:92861; MARPAT 135:92861
AΒ
     Title amino acid fluorides p-O2NC6H4SO2CH2CH2O2CNR1CHR2COF [R1 = H, R2 =
    H, iso-Pr, 2-methylpropyl, tert-butoxymethyl, benzyl, 2-(tert-
    butoxycarbonyl)ethyl, 4-(tert-butoxycarbamido)butyl or
     4-tert-butoxybenzyl] (Nsc-amino acid fluorides) were prepared by
     fluorinating Nsc-amino acids with cyanuric fluoride. Thus, 1 mmol
    Nsc-Val-OH in CH2Cl2 was treated with 3 mmol cyanuric fluoride and 1 mmol
     dry pyridine under nitrogen for 30 min to afford 82% Nsc-Val-F. The
    Nsc-amino acids fluorides were applied, without an activation step, to the
     solid-phase synthesis of peptides Leu-enkephalin, A-VI-5 peptide, and
     B-amyloid peptide.
ST
    nitrophenylsulfonylethoxycarbonyl amino acid fluoride prepn peptide
     coupling
IT
     Solid phase synthesis
        (peptide; preparation of (nitrophenylsulfonyl)ethoxycarbonyl amino acid
```

IT Peptides, preparation

RL: IMF (Industrial manufacture); PREP (Preparation)

(preparation of (nitrophenylsulfonyl)ethoxycarbonyl amino acid fluorides)

IT Amino acids, preparation

RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)

(preparation of (nitrophenylsulfonyl)ethoxycarbonyl amino acid fluorides)

IT 39194-96-2P 58822-25-6P, Leu-enkephalin 153247-40-6P

RL: IMF (Industrial manufacture); PREP (Preparation)

(preparation of (nitrophenylsulfonyl)ethoxycarbonyl amino acid fluorides)

IT 348621-98-7P 348621-99-8P 348622-00-4P 348622-01-5P 348622-02-6P

348622-03-7P 348622-04-8P 348622-05-9P

RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)

(preparation of (nitrophenylsulfonyl)ethoxycarbonyl amino acid fluorides)

IT 675-14-9, Cyanuric fluoride 35661-40-6D, Fmoc-L-phenylalanine, polyethylene glycol/polystyrene-bound 35661-60-0D, polyethylene

glycol/polystyrene-bound 71989-26-9D, polyethylene glycol/polystyrene-

bound 160422-18-4 160422-21-9 160422-23-1 160422-25-3

181763-90-6 181763-91-7 181763-93-9 181763-98-4

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of (nitrophenylsulfonyl)ethoxycarbonyl amino acid fluorides)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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IT 153247-40-6P

RL: IMF (Industrial manufacture); PREP (Preparation)

(preparation of (nitrophenylsulfonyl)ethoxycarbonyl amino acid fluorides)

RN 153247-40-6 HCAPLUS

CN L-Phenylalanine, L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L45 ANSWER 9 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:416788 HCAPLUS

DN 135:18553

ED Entered STN: 08 Jun 2001

TI Vaccine for the prevention and treatment of Alzheimer's and amyloid related diseases

IN Chalifour, Robert; Hebert, Lise; Kong, Xianqi; Gervais,
 Francine

PA Neurochem, Inc., Can.

SO PCT Int. Appl., 31 pp. CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K039-00

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CC
     15-2 (Immunochemistry)
FAN.CNT 2
     PATENT NO.
                       KIND DATE
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                                                                 DATE
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     WO 2001039796 A2 20010607 WO 2000-CA1413 20001129 WO 2001039796 A3 20011206
PΙ
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             LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
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NO 2002002531 A 20020712 NO 2002-2531
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                                                                  20020528
PRAI US 1999-168594P P
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    US 2000-724842
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CLASS
 PATENT NO.
              CLASS PATENT FAMILY CLASSIFICATION CODES
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WO 2001039796 ICM
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JP 2004500354 FTERM 4C085/AA03; 4C085/BB11; 4C085/CC32; 4C085/EE06;
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                       4C085/GG02; 4C085/GG03; 4C085/GG04; 4C085/GG08;
                       4C085/GG10; 4H045/AA10; 4H045/AA30; 4H045/BA01;
                       4H045/BA11; 4H045/BA12; 4H045/BA13; 4H045/BA14;
                        4H045/BA18; 4H045/BA19; 4H045/CA40; 4H045/EA31
AB
    The present invention relates to a stereochem. based "non-self" antigen
    vaccine for the prevention and/or treatment of Alzheimer's and other
    amyloid related diseases. The present invention provides a vaccine for
     the prevention and treatment of Alzheimer's and other amyloid related
     diseases, which overcomes the drawbacks associated with using naturally
    occurring peptides, proteins or immunogens.
ST
    vaccine Alzheimers disease amyloidosis D peptide antibody
IT
    Peptides, biological studies
    RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
        (all-D; vaccine for prevention and treatment of Alzheimer's and amyloid
        related diseases using all-D peptides that elicit immune response to
        amyloid protein)
TΤ
    Organelle
        (fibril; vaccine for prevention and treatment of Alzheimer's and
        amyloid related diseases using all-D peptides that elicit immune
        response to amyloid protein)
IT
    Alzheimer's disease
    Amyloidosis
    Self-association
    Vaccines
        (vaccine for prevention and treatment of Alzheimer's and amyloid
       related diseases using all-D peptides that elicit immune response to
       amyloid protein)
IT
    Antibodies
    RL: BAC (Biological activity or effector, except adverse); BPN
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(Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(vaccine for prevention and treatment of Alzheimer's and amyloid related diseases using all-D peptides that elicit immune response to amyloid protein)

## IT Amyloid

RL: BSU (Biological study, unclassified); BIOL (Biological study) ( $\beta$ -; vaccine for prevention and treatment of Alzheimer's and amyloid related diseases using all-D peptides that elicit immune response to amyloid protein)

IT 165196-29-2P 226707-64-8P 342877-53-6P 342877-54-7P 342877-52-5P 342877-55-8P 342877-56-9P 342877-57-0P 342877-58-1P 342877-59-2P 342877-60-5P 342877-61-6P 342877-62-7P 342877-63-8P 342877-64-9P 342877-65-0P 342877-66-1P 342877-67-2P 342877-68-3P **342877-69-4P** 342877-70-7P 342877-71-8P 342877-72-9P 342877-73-0P 342877-74-1P 342877-75-2P 342877-76-3P 342877-77-4P 342877-78-5P 342877-79-6P 342877-80-9P 342877-81-0P 342877-82-1P 342877-83-2P 342877-84-3P 342877-85-4P 342877-86-5P 342877-87-6P 342877-88-7P 342877-89-8P 342877-90-1P 342877-91-2P 342877-92-3P 342877-93-4P 342877-94-5P 342877-95-6P 342877-96-7P 342877-97-8P 342877-98-9P 342877-99-0P 342878-00-6P 342878-01-7P 342878-02-8P 342878-03-9P 342878-04-0P 342878-05-1P 342878-06-2P 342878-07-3P 342878-08-4P 342878-09-5P 342878-10-8P 342896-25-7P 342896-48-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(vaccine for prevention and treatment of Alzheimer's and amyloid related diseases using all-D peptides that elicit immune response to amyloid protein)

## IT 342877-55-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(vaccine for prevention and treatment of Alzheimer's and amyloid related diseases using all-D peptides that elicit immune response to amyloid protein)

## RN 342877-55-8 HCAPLUS

CN D-Alanine, D-lysyl-D-leucyl-D-valyl-D-phenylalanyl-D-phenylalanyl- (9CI) (CA INDEX NAME)

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DN
     134:125971
ED
     Entered STN: 02 Feb 2001
     Peptides containing N-substituted D-amino acids for preventing
TI
     β-strand association
     Stott, Kelvin
IN
PΑ
    UK
     PCT Int. Appl., 76 pp.
SO
     CODEN: PIXXD2
DT
     Patent
LA
    English
IC
     ICM C07K014-47
     ICS A61K038-17; A61P025-28; C07K007-06
CC
     1-12 (Pharmacology)
FAN.CNT 1
    WO 2001007474 Δ1
     PATENT NO.
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                                      APPLICATION NO.
                       A1 20010201 WO 2000-GB2923
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            SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
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     JP 2003505470
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20031106 AU 2000-63004
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    WO 2000-GB2923
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CLASS
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WO 2001007474 ICM
                       C07K014-47
                ICS
                       A61K038-17; A61P025-28; C07K007-06
     Chemical compds. and compns. are disclosed which comprise peptides composed
AB
     of D-enantiomers of amino acids and capable of binding to \beta-strand
     structures to form \beta-sheets, the peptides being selectively
     N\alpha-substituted to prevent further \beta-strand association The
    peptides are useful for preventing \beta-strand association. The capacity of
     all-D-[Ac--Leu-MeLeu-Leu-MeLeu-Arg-Arg-NH2] to inhibit aggregation of a
     synthetic peptide fragment corresponding to residues 11-25 of the
    Alzheimer Aß peptide into amyloid fibrils was determined
ST
    peptide deriv beta strand assocn inhibition; Alzheimer amyloid aggregation
     inhibition peptide
IT
     Proteins, general, biological studies
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (aggregation; peptides containing N-substituted D-amino acids for
       preventing \beta-strand association)
IT
    Cytotoxic agents
        (conjugates; peptides containing N-substituted D-amino acids for preventing
       β-strand association)
IΤ
    Antibodies
    Enzymes, biological studies
    Hormones, animal, biological studies
     Proteins, specific or class
    Transcription factors
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```
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (conjugates; peptides containing N-substituted D-amino acids for preventing
        β-strand association)
TT
     Biological transport
        (drug; peptides containing N-substituted D-amino acids for preventing
        β-strand association)
IT
     Electrostatic force
        (electrostatic and other non-covalent interactions; peptides containing
        N-substituted D-amino acids for preventing \beta-strand association)
IT
     Hydrophobicity
        (hydrophobic interaction; peptides containing N-substituted D-amino acids
        for preventing \beta-strand association)
IT
     Aggregation
     Anti-Alzheimer's agents
     Blood-brain barrier
     Chromophores
     Drug targeting
     Fluorescent substances
     Hydrogen bond
     Immobilization, biochemical
     Magnetic materials
     Molecular association
     Radioactive substances
     Spectroscopy
     Spin labels
        (peptides containing N-substituted D-amino acids for preventing
        β-strand association)
TΤ
     Peptides, biological studies
     RL: BAC (Biological activity or effector, except adverse); BPR (Biological
     process); BSU (Biological study, unclassified); THU (Therapeutic use);
     BIOL (Biological study); PROC (Process); USES (Uses)
        (peptides containing N-substituted D-amino acids for preventing
        β-strand association)
TТ
     Amino acids, biological studies
     RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
     BIOL (Biological study); OCCU (Occurrence)
        (peptides containing N-substituted D-amino acids for preventing
        β-strand association)
IT
     Amyloid
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (peptides containing N-substituted D-amino acids for preventing
        β-strand association)
     Conformation
TΫ́
        (protein; peptides containing N-substituted D-amino acids for preventing
        β-strand association)
IT
     Amyloid
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (β-; peptides containing N-substituted D-amino acids for preventing
        β-strand association)
TT
     Conformation
        (β-strand; peptides containing N-substituted D-amino acids for
        preventing \beta-strand association)
TΤ
     321909-16-4P
     RL: BAC (Biological activity or effector, except adverse); BPR (Biological
     process); BSU (Biological study, unclassified); PRP (Properties); SPN
     (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);
     PREP (Preparation); PROC (Process); USES (Uses)
        (peptides containing N-substituted D-amino acids for preventing
        β-strand association)
     56-40-6, Glycine, biological studies 56-41-7, L-Alanine, biological
IT
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56-87-1, L-Lysine, biological studies 60-18-4, L-Tyrosine,

studies

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biological studies
                          61-90-5, L-Leucine, biological studies 63-68-3,
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              71-00-1, L-Histidine, biological studies
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                          73-22-3, L-Tryptophan, biological studies
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     L-Isoleucine, biological studies
     147-85-3, L-Proline, biological studies 153-94-6, D-Tryptophan
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     157-06-2, D-Arginine
     328-38-1, D-Leucine
                                                 348-67-4, D-Methionine
                         338-69-2, D-Alanine
     351-50-8, D-Histidine
                             556-02-5, D-Tyrosine
                                                   556-02-5D, D-Tyrosine,
              632-20-2, D-Threonine
                                      640-68-6, D-Valine
                                                           673-06-3,
     derivs.
                       673-06-3D, D-Phenylalanine, derivs.
     D-Phenylalanine
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                  923-27-3, D-Lysine
                                      1783-96-6, D-Aspartic acid
     D-Cysteine
                                                                    2058-58-4,
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     RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
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        (peptides containing N-substituted D-amino acids for preventing
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                                          7553-56-2D, Iodine, isotopes,
IT
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     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (peptides containing N-substituted D-amino acids for preventing
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RE.CNT
              THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Chitnumsub, P; BIOORGANIC AND MEDICINAL CHEMISTRY 1999, V7(1), P39 HCAPLUS
(2) Doig, A; CHEM COMMUN (CAMBRIDGE) 1997, 22, P2153 HCAPLUS
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(4) Pallitto, M; BIOCHEMISTRY 1999, V38(12), P3570 HCAPLUS
```

- (5) Pharm Peptides Inc; WO 9628471 A 1996 HCAPLUS
- (6) Praecis Pharm Inc; WO 0052048 A 2000 HCAPLUS
- (7) Texas A & M University Syst; WO 9746547 A 1997 HCAPLUS
- (8) Tjernberg, L; JOURNAL OF BIOLOGICAL CHEMISTRY 1997, V272(19), P12601 MEDLINE
- 153247-40-6 IT
  - RL: PRP (Properties)

(unclaimed sequence; peptides containing N-substituted D-amino acids for preventing β-strand association)

- RN153247-40-6 HCAPLUS
- L-Phenylalanine, L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX CN NAME)

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ANSWER 11 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
AN
     2001:78414 HCAPLUS
DN
     134:141772
ED
     Entered STN: 02 Feb 2001
     Peptides containing N-substituted L-amino acids for preventing
ΤI
     β-strand association
IN
     Stott, Kelvin
PA
    UK
so
     PCT Int. Appl., 77 pp.
     CODEN: PIXXD2
DT
     Patent
     English
LΑ
IC
     ICM C07K014-47
     ICS A61K038-17; A61P025-28; C07K007-06
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PATENT NO.
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 WO 2001007473
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                       A61K038-17; A61P025-28; C07K007-06
AB
     Chemical compds. and compns. are disclosed which comprise peptides capable of
     binding to \beta-strand structures to form \beta-sheets, the peptides
     being selectively N\alpha-substituted to prevent further \beta-strand
     association The peptides are useful for preventing \( \beta \)-strand association. The
     capacity of Ac-Arg-MeArg-Leu-MeLeu-Phe-MePhe-NH2 to inhibit aggregation of
     a synthetic peptide fragment corresponding to residues 11-25 of the
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Alzheimer Aß peptide into amyloid fibrils was determined

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ST
     peptide deriv beta strand assocn inhibition; Alzheimer amyloid aggregation
     inhibition peptide
     Proteins, general, biological studies
IT
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (aggregation; peptides containing N-substituted L-amino acids for
        preventing β-strand association)
IT
     Cytotoxic agents
        (conjugates; peptides containing N-substituted L-amino acids for preventing
        β-strand association)
IT
     Antibodies
     Enzymes, biological studies
     Hormones, animal, biological studies
     Proteins, specific or class
     Transcription factors
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (conjugates; peptides containing N-substituted L-amino acids for preventing
        β-strand association)
IT
     Biological transport
        (drug; peptides containing N-substituted L-amino acids for preventing
        β-strand association)
TΤ
     Aggregation
     Anti-Alzheimer's agents
     Blood-brain barrier
     Chromophores
     Drug targeting
     Fluorescent substances
     Immobilization, biochemical
     Magnetic materials
     Molecular association
     Molecular modeling
     Radioactive substances
     Spectroscopy
     Spin labels
        (peptides containing N-substituted L-amino acids for preventing
        β-strand association)
     Peptides, biological studies
IT
     RL: BAC (Biological activity or effector, except adverse); BPR (Biological
     process); BSU (Biological study, unclassified); THU (Therapeutic use);
     BIOL (Biological study); PROC (Process); USES (Uses)
        (peptides containing N-substituted L-amino acids for preventing
        \beta-strand association)
IT
    Amino acids, biological studies
     RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
    BIOL (Biological study); OCCU (Occurrence)
        (peptides containing N-substituted L-amino acids for preventing
        β-strand association)
IT
     Amyloid
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (peptides containing N-substituted L-amino acids for preventing
        β-strand association)
TΨ
    Conformation
        (protein; peptides containing N-substituted L-amino acids for preventing
        \beta-strand association) .
TT
    Amyloid
    RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (β-; peptides containing N-substituted L-amino acids for preventing
        β-strand association)
TΤ
    Conformation
        (β-strand; peptides containing N-substituted L-amino acids for
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preventing β-strand association)

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Amino acids, biological studies
IΤ
     RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
     BIOL (Biological study); OCCU (Occurrence)
        (D-; peptides containing N-substituted L-amino acids for preventing
        B-strand association)
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     (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);
     PREP (Preparation); PROC (Process); USES (Uses)
        (peptides containing N-substituted L-amino acids for preventing
        β-strand association)
IT
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     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); BIOL (Biological study)
        (peptides containing N-substituted L-amino acids for preventing
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                        73-22-3, L-Tryptophan, biological studies
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        β-strand association)
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     RL: BPR (Biological process); BSU (Biological study, unclassified); PRP
     (Properties); BIOL (Biological study); PROC (Process)
        (peptides containing N-substituted L-amino acids for preventing
        β-strand association)
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     2564-83-2, TEMPO
TΤ
     biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (peptides containing N-substituted L-amino acids for preventing
        β-strand association)
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        (unclaimed protein sequence; peptides containing N-substituted L-amino
        acids for preventing \beta-strand association)
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     RL: PRP (Properties)
        (unclaimed sequence; peptides containing N-substituted L-amino acids for
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RE.CNT
              THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Chitnumsub, P; BIOORGANIC AND MEDICINAL CHEMISTRY 1999, V7(1), P39 HCAPLUS
(2) Doig, A; CHEM COMMUN (CAMBRIDGE) 1997, 22, P2153 HCAPLUS
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(4) Karolinska Innovations Ab; WO 9721728 A 1997 HCAPLUS
(5) Moehle, K; JOURNAL OF PEPTIDE RESEARCH 1998, V51(1), P19
(6) Pallitto, M; BIOCHEMISTRY 1999, V38(12), P3570 HCAPLUS
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(7) Pharm Peptides Inc; WO 9628471 A 1996 HCAPLUS

(8) Texas A & M University Syst; WO 9746547 A 1997 HCAPLUS

IT 153247-40-6

RL: PRP (Properties)

(unclaimed sequence; peptides containing N-substituted L-amino acids for preventing  $\beta$ -strand association)

RN 153247-40-6 HCAPLUS

CN L-Phenylalanine, L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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L45 ANSWER 12 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
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AN 2000:861520 HCAPLUS

DN 134:28433

ED Entered STN: 08 Dec 2000

TI Prevention and treatment of amyloidogenic disease

IN Schenk, Dale B.; Bard, Frederique; Vasquez, Nicki J.; Yednock, Ted

PA Neuralab Limited, Bermuda

SO PCT Int. Appl., 143 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K039-395

ICS A61K038-17; A61K039-39; A61K039-00; G01N033-68; A61K048-00; A61P025-28; C07K016-18; C07K014-47

CC 15-2 (Immunochemistry)

Section cross-reference(s): 8, 63

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WO 2000072880
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AB
    The invention provides improved agents and methods for treatment of
    diseases associated with amyloid deposits of A\beta in the brain of a
    patient. Such methods entail administering agents that induce a
    beneficial immunogenic response against the amyloid deposit. The methods
    are useful for prophylactic and therapeutic treatment of Alzheimer's
    disease. Preferred agents including N-terminal fragments of AB and
    antibodies binding to the same.
ST
    amyloid beta epitope antibody Alzheimer disease; amyloidogenic disease
    amyloid precursor protein antibody
IT
    Phagocytosis
        (Fc receptor-mediated; N-terminal fragments of amyloid β and
       antibodies for prevention and treatment of amyloidogenic disease)
IT
    Immunoglobulins
    RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
       (G1; N-terminal fragments of amyloid \beta and antibodies for
       prevention and treatment of amyloidogenic disease)
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RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL

IT

Immunoglobulins

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(Biological study); USES (Uses)
        (G2; N-terminal fragments of amyloid \beta and antibodies for
        prevention and treatment of amyloidogenic disease)
     Immunoglobulins
TΤ
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (G3; N-terminal fragments of amyloid \beta and antibodies for
        prevention and treatment of amyloidogenic disease)
TТ
     Immunoglobulins
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (G4; N-terminal fragments of amyloid \beta and antibodies for
        prevention and treatment of amyloidogenic disease)
     Alzheimer's disease
TΤ
     Animal tissue
     Blood
     Down's syndrome
     Epitopes
     Labels
     Mammal (Mammalia)
     NMR tomography
     Phagocyte
     Protein sequences
     Susceptibility (genetic)
        (N-terminal fragments of amyloid \beta and antibodies for prevention
        and treatment of amyloidogenic disease)
TΤ
     Immunoglobulin receptors
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (N-terminal fragments of amyloid \beta and antibodies for prevention
        and treatment of amyloidogenic disease)
IT
     Amyloid precursor proteins
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (N-terminal fragments of amyloid \beta and antibodies for prevention
        and treatment of amyloidogenic disease)
TΤ
     Antigens
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (N-terminal fragments of amyloid \beta and antibodies for prevention
        and treatment of amyloidogenic disease)
IT
     Fusion proteins (chimeric proteins)
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (N-terminal fragments of amyloid \beta and antibodies for prevention
        and treatment of amyloidogenic disease)
IΤ
     Peptides, biological studies
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (N-terminal fragments of amyloid \beta and antibodies for prevention
        and treatment of amyloidogenic disease)
IT
     Polynucleotides
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (N-terminal fragments of amyloid \beta and antibodies for prevention
        and treatment of amyloidogenic disease)
ΙT
     Proteins, general, biological studies
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (N-terminal fragments of amyloid \beta and antibodies for prevention
        and treatment of amyloidogenic disease)
IT
     RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES
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(Uses)

(N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Antibodies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Immunostimulants

(adjuvants, Freund's incomplete; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Immunostimulants

(adjuvants; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Diagnosis

(agents, kit; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Brain, disease

Disease, animal

(amyloidogenic; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Mouse

(antibody; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Drug delivery systems

(carriers; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Mental disorder

(cognitive; N-terminal fragments of amyloid  $\beta$  and antibodies tor prevention and treatment of amyloidogenic disease)

IT Amyloid

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)

(deposit; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Test kits

(diagnostic; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Extracellular matrix

(disease; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Cognition

(disorder; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Immunoglobulins

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (fragments; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Immunoglobulins

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(heavy chains; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Diagnosis

(immunodiagnosis; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Drug delivery systems

(injections, i.m.; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Drug delivery systems

(injections, i.v.; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Drug delivery systems

(injections, s.c.; N-terminal fragments of amyloid  $\beta$  and

antibodies for prevention and treatment of amyloidogenic disease) Paramagnetic materials TΤ (label; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease) Immunoglobulins IT RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (light chains; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease) Antibodies ITRL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (monoclonal; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease) TΤ Lipid A RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (monophosphates; N-terminal fragments of amyloid β and antibodies for prevention and treatment of amyloidogenic disease) Drug delivery systems IT (nasal, intra-; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease) IT Drug delivery systems (oral; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease) IT Disease, animal (proliferative; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease) TT Drug delivery systems (solns., i.p.; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease) IT Drug delivery systems (sustained-release; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease) ΙT Infection Inflammation Neoplasm (tissue sample; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease) ITDrug delivery systems (topical; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease) IT Amyloid RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  $(\beta$ -; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease) IT 107761-42-2, Glycopeptide (human clone 9-110 amyloid A4 peptide moiety) 118427-80-8 214550-64-8 250741-37-8 268202-35-3 310901-07-6 RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease) IT 141256-04-4, QS-21 310901-08-7 312273-37-3 RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease) TT 214550-60-4 226917-45-9 311818-22-1 178949-81-0 RL: PRP (Properties) (Unclaimed; prevention and treatment of amyloidogenic disease) IΤ 109796-61-4 110162-70-4 111750-71-1 118821-52-6 122630-93-7 123232-50-8 126779-13-3 126779-14-4 128124-74-3 144500-61-8

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RL: PRP (Properties)

(unclaimed sequence; prevention and treatment of amyloidogenic disease) 176390-00-4

RL: PRP (Properties)

(unclaimed sequence; prevention and treatment of amyloidogenic disease)

RN176390-00-4 HCAPLUS

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L-Phenylalanine, L-α-glutamyl-L-valyl-L-histidyl-L-histidyl-L-CN glutaminyl-L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

PAGE 1-B

WO 2000068263

ICM

C07K014-47

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L45 ANSWER 13 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
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    Entered STN: 21 Nov 2000
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    Stereoselective antifibrillogenic peptides and peptidomimetics thereof
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    Chalifour, Robert; Gervais, Francine; Gupta,
    Ajay
PΑ
    Neurochem, Inc., Can.
so
    PCT Int. Appl., 46 pp.
    CODEN: PIXXD2
DT
    Patent
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    English
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    ICS A61K038-17; G01N033-68; A61P025-28; C12N005-00; A61K051-00
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CLASS
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ICS A61K038-17; G01N033-68; A61P025-28; C12N005-00; A61K051-00

AB The present invention relates to antifibrillogenic agents for inhibiting amyloidosis and/or for cytoprotection for the treatment of amyloidosis disorders. These agents include peptides, isomers thereof and peptidomimetic compds. thereof. These agents comprise a peptide having a sequence identified from the glycosaminoglycan (GAG) binding region and the prot-prot interaction region of the amyloid protein. The peptide has at least one D-amino acid isomer substitution. The invention also relates to the peptide bound to a label for in vivo imaging of amyloid deposits. ST antifibrillogenic peptidomimetic amyloid protein amyloidosis; retroinverso

peptide antifibrillogenic agent Alzheimer disease

TТ Drugs

> (antifibrillogenic peptides; stereoselective antifibrillogenic peptides and peptidomimetics)

ΙT Peptides, biological studies

> RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antifibrillogenic; stereoselective antifibrillogenic peptides and peptidomimetics)

ITDrug delivery systems

> (carriers; stereoselective antifibrillogenic peptides and peptidomimetics)

TT Transplant and Transplantation

(cell; stereoselective antifibrillogenic peptides and peptidomimetics)

TT Peptides, biological studies

> RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(conjugates; stereoselective antifibrillogenic peptides and peptidomimetics)

TΤ Amyloid

> RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)

(deposit detection; stereoselective antifibrillogenic peptides and peptidomimetics)

Organelle TT

(fibril, formation inhibition; stereoselective antifibrillogenic peptides and peptidomimetics)

Amino acids, biological studies TT

RL: BSU (Biological study, unclassified); BIOL (Biological study) (hydrophobic; stereoselective antifibrillogenic peptides and peptidomimetics)

TΤ Peptides, biological studies

> RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(retro-inverso; stereoselective antifibrillogenic peptides and peptidomimetics)

IT Alzheimer's disease

Amyloidosis

Imaging agents

Labels

Mammal (Mammalia)

Peptidomimetics

Protein sequences

(stereoselective antifibrillogenic peptides and peptidomimetics)

TΤ Animal cell

> (transplant; stereoselective antifibrillogenic peptides and peptidomimetics)

TT Amino acids, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(D-; stereoselective antifibrillogenic peptides and peptidomimetics)

IT 14133-76-7, Technetium-99, biological studies

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (label; stereoselective antifibrillogenic peptides and peptidomimetics) IT 50-99-7, Glucose, biological studies 63-91-2, Phenylalanine, biological RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (linker; stereoselective antifibrillogenic peptides and peptidomimetics) IT 107761-42-2, Glycopeptide (human clone 9-110 amyloid A4 peptide moiety) RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (stereoselective antifibrillogenic peptides and peptidomimetics) IT 153247-40-6D, analogs 176390-09-3D, analogs 176390-19-5D, analogs 176390-21-9D, analogs 190775-14-5D , analogs 206198-57-4D, analogs 307299-71-4D, analogs **307299-72-5D**, analogs **307299-73-6D**, analogs **307299-74-7D** , analogs 307299-75-8D, analogs 307299-76-9D, analogs **307299-77-0D**, analogs 307299-78-1D, analogs RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (stereoselective antifibrillogenic peptides and peptidomimetics) IT 153247-40-6D, analogs RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (stereoselective antifibrillogenic peptides and peptidomimetics) RN 153247-40-6 HCAPLUS CN L-Phenylalanine, L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

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L45
     ANSWER 14 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
AN
     2000:96000 HCAPLUS
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     132:146648
ED
     Entered STN: 10 Feb 2000
     Peptide inhibitors of \beta-amyloid toxicity
TI
IN
     Kiessling, Laura L.; Murphy, Regina M.
PΑ
     Wisconsin Alumni Research Foundation, USA
SO
     U.S., 15 pp.
     CODEN: USXXAM
DT
     Patent
LΑ
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     ICM A61K038-00
IC
NCL
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CC
     1-11 (Pharmacology)
     Section cross-reference(s): 63
FAN.CNT 1
     PATENT NO.
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                       C07K005/10B; C07K014/47A3
US 6022859
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   A \beta-amyloid inhibitor is disclosed which is of relevance to the
     treatment of Alzheimer's disease. In one embodiment, this inhibitor
     comprises a recognition element that interacts specifically with
     \beta-amyloid peptide and a disrupting element that alters \beta-amyloid
     aggregation. In a preferable form of the present invention, the inhibitor
     is a peptide.
    beta amyloid toxicity inhibitor Alzheimer disease
ST
IT
    Anti-Alzheimer's agents
     Cytotoxicity
     Protein sequences
        (peptide inhibitors of \beta-amyloid toxicity)
IT
     Peptides, biological studies
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (peptide inhibitors of \beta-amyloid toxicity)
TΤ
     Peptides, biological studies
     RL: BPR (Biological process); BSU (Biological study, unclassified); PRP
     (Properties); BIOL (Biological study); PROC (Process)
        (recognition; peptide inhibitors of β-amyloid toxicity)
IT
    Amyloid
    RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
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RE.CNT
             THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Anon; WO 9425043 1994 HCAPLUS
(2) Anon; WO 9520973 1995 HCAPLUS
(3) Anon; WO 9531210 1995 HCAPLUS
(4) Anon; WO 9628471 1996 HCAPLUS
(5) Dayhoff; Atlas of Protein Sequence and Structure 1972, V5, P89
(6) Ghanta, J; J Biol Chem 1996, V271(47), P29525029528
(7) Hughes; Proc Nat'l Acad Sci USA 1996, V93, P2065 HCAPLUS
(8) Katz; US 5716614 1998 HCAPLUS
(9) Lars, O; J Biol Chem 1996, V271(15), P8545
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CN
    L-Phenylalanine, L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX
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ANSWER 15 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN L45 AN 1999:278142 HCAPLUS DN 131:110884 Entered STN: 06 May 1999 ED Modified-Peptide Inhibitors of Amyloid β-Peptide Polymerization TI Findeis, Mark A.; Musso, Gary M.; Arico-Muendel, Christopher C.; Benjamin, ΑU Howard W.; Hundal, Arvind M.; Lee, Jung-Ja; Chin, Joseph; Kelley, Michael; Wakefield, James; Hayward, Neil J.; Molineaux, Susan M. CS PRAECIS Pharm. Inc., Cambridge, MA, 02139-1572, USA SO Biochemistry (1999), 38(21), 6791-6800 CODEN: BICHAW; ISSN: 0006-2960 PB American Chemical Society DT Journal English LΑ CC 1-3 (Pharmacology) Cellular toxicity resulting from nucleation-dependent polymerization of amyloid AB  $\beta$ -peptide (A $\beta$ ) is considered to be a major and possibly the primary component of Alzheimer's disease (AD). Inhibition of AB polymerization has thus been identified as a target for the development of therapeutic agents for the treatment of AD. The intrinsic affinity of A $\beta$  for itself suggested that A $\beta$ -specific interactions could be adapted to the development of compds. that would bind to  $A\beta$  and prevent it from polymerizing Aβ-derived peptides of fifteen residues were found to be inhibitory of  $A\beta$  polymerization. The activity of these peptides was subsequently enhanced through modification of their amino termini with specific organic reagents. Addnl. series of compds. prepared to probe structural requirements for activity allowed reduction of the size of the inhibitors and optimization of the AB-derived peptide portion to afford a lead compound, cholyl-Leu-Val-Phe-Phe-Ala-OH (PPI-368), with potent polymerization inhibitory activity but limited biochem. stability. The corresponding all-D-amino acyl analog peptide acid (PPI-433) and amide (PPI-457) retained inhibitory activity and were both stable in monkey cerebrospinal fluid for 24 h. amyloid beta polymn inhibitor Alzheimer disease ST IT Structure-activity relationship (anti-Alzheimer's drugs; modified peptide inhibitors of amyloid β-peptide polymerization and stability in monkey CSF) IT Biological transport

(drug; modified peptide inhibitors of amyloid β-peptide polymerization and stability in monkey CSF)

IT Anti-Alzheimer's agents

Cerebrospinal fluid

(modified peptide inhibitors of amyloid \beta-peptide polymerization and stability in monkey CSF)

IT Amyloid

> RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

( $\beta$ -; modified peptide inhibitors of amyloid  $\beta$ -peptide polymerization and stability in monkey CSF)

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                35404-50-3
                             39098-97-0, 2-Thiopheneacetyl chloride
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RE.CNT
              THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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- IT 153247-40-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(modified peptide inhibitors of amyloid  $\beta\text{-peptide}$  polymerization and stability in monkey CSF)

- RN 153247-40-6 HCAPLUS
- CN L-Phenylalanine, L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

- L45 ANSWER 16 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
- AN 1999:166639 HCAPLUS
- DN 130:209984
- ED Entered STN: 15 Mar 1999
- TI Synthesis of cyclosporin A conjugates for treatment of neurological disorders
- IN Rich, Daniel H.; Solomon, Michael E.
- PA Wisconsin Alumni Research Foundation, USA
- SO PCT Int. Appl., 129 pp. CODEN: PIXXD2
- DT Patent
- LA English
- IC ICM C07K007-64 ICS A61K038-13
- CC 34-3 (Amino Acids, Peptides, and Proteins)
  Section cross-reference(s): 1

FAN.CNT 2

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	PATENT NO.						D :	DATE		APPLICATION NO.						D.			
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ΡI	WO	0 9910374			A1		19990304		WO 1998-US17544						19980825 <				
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			ΚP,	KR,	ΚZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MD,	MG,	MK,	MN,	MW,	MX,	
			NO,	NZ,	PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	TJ,	TM,	TR,	TT,	
			UA,	UG,	US,	UΖ,	VN,	YU,	ZW,	AM,	AZ,	BY,	KG,	KZ,	MD,	RU.	TJ.	TM	

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             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
             CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     AU 9892038
                         A1
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                                         AU 1998-92038
                                                                  19980825 <--
     US 6316405
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                                           US 1999-242724
                                                                19990222 <--
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     WO 1998-US17544
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                               19980825 <--
CLASS
                CLASS PATENT FAMILY CLASSIFICATION CODES
 PATENT NO.
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                       _______
 WO 9910374
                ICM
                       C07K007-64
                ICS
                       A61K038-13
 WO 9910374
                ECLA
                       C07K007/64A
os
     MARPAT 130:209984
AB
     Cyclosporin A (CsA) conjugates, cyclo(V-Abu-W-X-Val-X'-Y(Z)-D-Ala-MeLeu-
     MeLeu-MeVal) [V = MeLeu(3-OH), MeLeu, MeSer, MeSer-PG, MeThr, MeThr-PG,
     where PG is a side-chain protecting group; W = D-N-Me amino acid or
     N-methylglycyl residue; X, X' = N-methylleucinyl or N-methylalanyl
     residue; Y = lysyl, homo-lysyl, ornithinyl, lysyl-PG, homo-lysyl-PG, or
     ornithinyl-PG residue; Z is a polypeptide comprising 5 or more contiquous
     residues of A\beta peptide], were prepared for the treatment of neurol.
     disorders. Thus, the synthesis of Ac-EKLVFF-NH2/[MeLeu(3-OH)1,D-
     MeAla4,6,Lys7]CsA conjugate is described.
ST
     cyclosporin A conjugate prepn treatment neurol disorder
IT
     Nervous system
        (disease; synthesis of cyclosporin A conjugates for treatment of
        neurol. disorders)
IT
     Peptides, preparation
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (synthesis of cyclosporin A conjugates for treatment of neurol.
        disorders)
IT
     78-84-2, Isobutyraldehyde 100-83-4, 3-Hydroxybenzaldehyde
     tert-Butyl chloroacetate 598-21-0, Bromoacetyl bromide 624-83-9,
     Methyl isocyanate 7693-46-1, p-Nitrophenyl chloroformate
     26250-84-0 28276-08-6, 1,1-Dimethylpropylmagnesium chloride
     59865-13-3, Cyclosporin a 90719-32-7 90878-19-6, Phenethylmagnesium
    chloride
               220871-31-8 220903-92-4 220903-96-8 220904-02-9
     220904-03-0 220904-04-1
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     RL: RCT (Reactant); RACT (Reactant or reagent)
        (synthesis of cyclosporin A conjugates for treatment of neurol.
        disorders)
TT
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                                                 220871-46-5P
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     220903-98-0P
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                                  220904-00-7P
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     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (synthesis of cyclosporin A conjugates for treatment of neurol.
        disorders)
IT
     104324-15-4P
                   220871-19-2P
                                  220871-49-8P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (synthesis of cyclosporin A conjugates for treatment of neurol.
        disorders)
IT
    220904-07-4P
                   220904-08-5P
                                  220904-09-6P
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                                                                220904-11-0P
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RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(synthesis of cyclosporin A conjugates for treatment of neurol. disorders)

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD RE

- (1) Avail; DISS ABSTR INT B 1998, V59(2), P671
- (2) Edward, S; The design and synthesis of novel dual inhibitor cyclosporin A conjugates 1997, P397
- (3) Guilford Pharm Inc; WO 9718828 A 1997 HCAPLUS
- (4) Sandoz Ag; WO 8602080 A 1986 HCAPLUS
- (5) Solomon, M; 212TH AMERICAN CHEMICAL SOCIETY NATIONAL MEETING 1996
- (6) Solomon, M; ABSTRACTS OF PAPERS AMERICAN CHEMICAL SOCIETY 1996, V212, P1
- (7) Wisconsin Alumni Res Found; WO 9606857 A 1996 HCAPLUS
- IT 220904-02-9

RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of cyclosporin A conjugates for treatment of neurol.
disorders)

RN 220904-02-9 HCAPLUS

CN L-Phenylalanine, N6-[[(2-chlorophenyl)methoxy]carbonyl]-N2-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

- L45 ANSWER 17 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
- AN 1999:148185 HCAPLUS
- DN 130:347290
- ED Entered STN: 09 Mar 1999
- TI Recognition sequence design for peptidyl modulators of  $\beta$ -amyloid aggregation and toxicity
- AU Pallitto, Monica M.; Ghanta, Jyothi; Heinzelman, Peter; Kiessling, Laura L.; Murphy, Regina M.
- CS Departments of Chemical Engineering and Chemistry, University of Wisconsin, Madison, WI, 53706, USA
- SO Biochemistry (1999), 38(12), 3570-3578 CODEN: BICHAW; ISSN: 0006-2960
- PB American Chemical Society
- DT Journal
- LA English
- CC 1-11 (Pharmacology)
- AB β-Amyloid (Aβ), the primary protein component of Alzheimer's plaques, is neurotoxic when aggregated into fibrils. We have devised a modular strategy for generating compds. that inhibit Aβ toxicity,

liu - 10 / 009122 based on linking a recognition element for AB to a disrupting element designed to interfere with AB aggregation. One such compound, with the 15-25 sequence of  $A\beta$  as the recognition element and a lysine hexamer as the disrupting element, altered Aß aggregation kinetics and protected cells from Aβ toxicity [Ghanta et al. (1996) J. Biol. Chemical 271, 29525]. To optimize the recognition element, peptides of 4-8 residues composed of overlapping sequences within the 15-25 domain were synthesized, along with hybrid compds. containing those recognition sequences coupled to a lysine hexamer. None of the recognition peptides altered Aβ aggregation kinetics and only two, KLVFF and KLVF, had any protective effect against AB toxicity. The hybrid peptide KLVFF-KKKKKK dramatically altered AB aggregation kinetics and aggregate morphol. and provided significantly improved protection against Aβ toxicity compared to the recognition peptide alone. In contrast, FAEDVG-KKKKKK possessed only modest inhibitory activity and had no marked effect on Aß aggregation. The scrambled sequence VLFKF was nearly as effective a recognition domain as KLVFF, suggesting the hydrophobic characteristics of the recognition sequence are critical None of the cytoprotective peptides prevented AB aggregation; rather, they increased aggregate size and altered aggregate morphol. These results suggest that coupling recognition with disrupting elements is an effective generalizable strategy for the creation of Aß inhibitors. Significantly, prevention of  $A\beta$  aggregation may not be required for prevention of toxicity. beta amyloid aggregation inhibitor recognition peptide Alzheimer Alzheimer's disease Cytotoxicity Drug design Hydrophobicity Molecular recognition (recognition sequence design for peptidyl modulators of  $\beta\text{-amyloid}$ aggregation and toxicity) Amyloid precursor proteins RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (recognition sequence design for peptidyl modulators of  $\beta$ -amyloid aggregation and toxicity) Amyloid

IT

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IT

IT

RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)

 $(\beta$ -; recognition sequence design for peptidyl modulators of  $\beta$ -amyloid aggregation and toxicity)

ITPeptides, biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(β-amyloid inhibitors; recognition sequence design for peptidyl modulators of  $\beta$ -amyloid aggregation and toxicity)

ΙT 153247-40-6P 176390-18-4P **176390-19-5P** 184951-41-5P 184951-43-7P 224645-03-8P 224645-04-9P 224645-06-1P 224645-07-2P 224645-08-3P 224645-09-4P 224645-10-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(recognition sequence design for peptidyl modulators of β-amyloid aggregation and toxicity)

RE.CNT THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD RE

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- (2) Busciglio, J; Neurobiol Aging 1992, V13, P609 HCAPLUS
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- IT 153247-40-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(recognition sequence design for peptidyl modulators of  $\beta\text{-amyloid}$  aggregation and toxicity)

- RN 153247-40-6 HCAPLUS
- CN L-Phenylalanine, L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

(51) Wujek, J; Neurobiol Aging 1996, V17, P107 HCAPLUS

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ANSWER 18 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
AN
     1999:21679 HCAPLUS
DN
     130:95847
ED
     Entered STN: 12 Jan 1999
ΤI
     Preparation of amyloid \beta peptides and derivatives that modulate
     β-amyloid aggregation
IN
     Findeis, Mark A.; Benjamin, Howard; Garnick, Marc B.; Gefter, Malcolm L.;
     Hundal, Arvind; Kasman, Laura; Musso, Gary; Signer, Ethan R.; Wakefield,
     James; Reed, Michael; Molineaux, Susan; Kubasek, William; Chin, Joseph;
     Lee, Jung-Ja; Kelley, Michael
PA
     Praecis Pharmaceuticals, Inc., USA
SO
     U.S., 52 pp., Cont.-in-part of U.S. Ser. No. 404,831.
     CODEN: USXXAM
DT
     Patent
LA
     English
IC
     ICM C07K014-435
     ICS C07K007-08
NCL
     514002000
     34-3 (Amino Acids, Peptides, and Proteins)
     Section cross-reference(s): 1
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                                DATE
                                             APPLICATION NO.
                                                                    DATE
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PΙ
     US 5854204
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                                19981229
                                             US 1996-612785
                                                                     19960314 <--
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                                                                     19950314 <--
     US 5854215
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     AU 1997-42387
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CLASS
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                 CLASS PATENT FAMILY CLASSIFICATION CODES
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                        C07K007-08
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 US 5854204
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                        C07K014/47A3
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 US 5817626
                 ECLA
                        C07K014/47A3
 US 5854215
                 ECLA
                        C07K014/47A3
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AB Compds. that modulate the aggregation of amyloidogenic proteins or peptides are disclosed. The modulators of the invention can promote amyloid aggregation or, more preferably, can inhibit natural amyloid aggregation. In a preferred embodiment, the compds. modulate the aggregation of natural  $\beta$  amyloid peptides ( $\beta$ -AP). In a preferred embodiment, the  $\beta$  amyloid modulator compds. of the invention are comprised of an A $\beta$  aggregation core domain and a

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(7) Anon; WO 9505604 1995 HCAPLUS (8) Anon; WO 9512815 1995 HCAPLUS

modifying group coupled thereto such that the compound alters the aggregation or inhibits the neurotoxicity of natural  $\beta$  amyloid peptides when contacted with the peptides. Furthermore, the modulators are capable of altering natural  $\beta$ -AP aggregation when the natural eta-APs are in a molar excess amount relative to the modulators. Pharmaceutical compns. comprising the compds. of the invention, and diagnostic and treatment methods for amyloidogenic diseases using the compds. of the invention, are also disclosed. amyloid peptide aggregation inhibitor prepn Alzheimer treatment Amyloidosis Anti-Alzheimer's agents (preparation of amyloid  $\beta$  peptides and derivs. that modulate β-amyloid aggregation) Amyloid RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)  $(\beta$ -; preparation of amyloid  $\beta$  peptides and derivs. that modulate β-amyloid aggregation) 81-25-4, Cholic acid RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses) (preparation of amyloid  $\beta$  peptides and derivs. that modulate β-amyloid aggregation) 123529-23-7P **153247-40-6P** 156858-22-9P 182912-78-3P 183745-73-5P 183745-74-6P 183745-77-9P 183745-79-1P 183745-81-5P 183745-84-8P 183745-86-0P 183745-88-2P 183745-82-6P 183745-90-6P 183745-92-8P 183746-04-5P 183746-05-6P 183746-07-8P 183746-08-9P 183746-09-0P 183746-10-3P 183746-11-4P 183746-12-5P 183746-13-6P 183746-14-7P 183746-15-8P 183746-16-9P 183746-19-2P 183746-20-5P 183746-17-0P 183746-18-1P 183746-22-7P 183746-23-8P 183746-24-9P 183746-21-6P 183746-26-1P 183746-27-2P 183746-28-3P 183746-33-0P 183746-30-7P 183746-31-8P 183746-36-3P 183746-44-3P 183746-48-7P 183746-50-1P 183746-42-1P 183746-53-4P 183746-55-6P 183746-58-9P 183746-61-4P 183746-63-6P 183746-65-8P 183746-66-9P 183746-67-0P 183746-68-1P 183746-69-2P 183746-71-6P 183746-73-8P 183746-75-0P 183746-77-2P 183746-79-4P 183746-80-7P 183746-81-8P 183746-82-9P 183746-84-1P 183746-87-4P 183746-89-6P 183746-85-2P 183746-91-0P 183746-93-2P 183746-94-3P 183746-95-4P 183746-96-5P 183746-97-6P 183746-98-7P 183747-00-4P 183746-99-8P 183903-86-8P 183903-87-9P 183906-01-6P 183906-03-8P 183906-04-9P 183906-05-0P 183906-07-2P 183906-09-4P 183906-10-7P 183906-12-9P 183906-14-1P 184051-28-3P 184051-29-4P 184051-30-7P 184051-31-8P 184051-32-9P 184051-33-0P 219127-34-1P 219127-35-2P 219127-36-3P 219127-38-5P 219127-40-9P 219127-41-0P 219127-42-1P **219127-44-3P** 219127-49-8P 219127-50-1P 219127-55-6P 219127-52-3P 219127-56-7P RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of amyloid  $\beta$  peptides and derivs. that modulate β-amyloid aggregation) THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD RE.CNT 24 (1) Anon; EP 554887 A1 1993 HCAPLUS (2) Anon; WO 9304194 1993 HCAPLUS (3) Anon; WO 9428412 1994 HCAPLUS (4) Anon; EP 641861 A1 1995 HCAPLUS (5) Anon; EP 681844 A1 1995 HCAPLUS (6) Anon; WO 9505394 1995 HCAPLUS

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- (24) Roberts; US 5470951 1995 HCAPLUS
- IT 153247-40-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of amyloid  $\beta$  peptides and derivs. that modulate  $\beta$ -amyloid aggregation)

RN 153247-40-6 HCAPLUS

CN L-Phenylalanine, L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L45 ANSWER 19 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1998:197424 HCAPLUS

DN 128:266268

ED Entered STN: 06 Apr 1998

TI Identification of agents that protect against inflammatory injury to neurons

IN Giulian, Dana J.

PA Baylor College of Medicine, USA; Giulian, Dana J.

SO PCT Int. Appl., 149 pp. CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K049-00

ICS G01N031-00; G01N033-48; G01N033-53; G01N033-567; G01N033-569

CC 1-11 (Pharmacology)

Section cross-reference(s): 63

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                       G01N033-569
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US 6043283
                ECLA
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OS
    MARPAT 128:266268
    Methods are disclosed for identifying agents that inhibit the toxic
AB
    effects of neurotoxins on neurons from plaque component-activated
    mononuclear phagocytes. Also disclosed are methods for identifying agents
    that inhibit mononuclear phagocyte-plaque component complex formation,
    plaque component activation of mononuclear phagocytes, and plaque
    component-induced neurotoxicity of mononuclear phagocytes. The invention
    is also directed to agents and pharmaceutical compns. obtained by the
    identification methods described. Addnl., the invention describes methods
    for using tyramine compds. to inhibit the toxic effects of neurotoxins and
    methods to treat and diagnose neurodegenerative diseases and disorders.
ST
    neuron inflammatory injury neuroprotectant identification; mononuclear
    phagocyte plaque component neurotoxicity neuroprotection;
    neurodegenerative disease diagnosis therapeutic; tyramine compd
    neuroprotectant
TT
    Apolipoproteins
    RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (A; identification of agents that protect against inflammatory injury
       to neurons)
IT
    AIDS (disease)
    AIDS (disease)
       (AIDS dementia complex; identification of agents that protect against
       inflammatory injury to neurons)
IT
    Mental disorder
    Mental disorder
        (AIDS dementia; identification of agents that protect against
       inflammatory injury to neurons)
    Brain, disease
IT
    Prion diseases
        (Creutzfeldt-Jakob, plaque component from; identification of agents
       that protect against inflammatory injury to neurons)
TΤ
    Apolipoproteins
    RL: BPR (Biological process); BSU (Biological study, unclassified); PUR
     (Purification or recovery); BIOL (Biological study); PREP (Preparation);
    PROC (Process)
       (E; identification of agents that protect against inflammatory injury
       to neurons)
IT
    Apolipoproteins
    RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
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(Biological study); PROC (Process)

(Lp(a); identification of agents that protect against inflammatory injury to neurons) ITGlutamate receptors RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (NMDA-binding; identification of agents that protect against inflammatory injury to neurons) IT mRNA RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (Scavenger receptor II; identification of agents that protect against inflammatory injury to neurons) TΤ Phenols, biological studies Phenols, biological studies RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (amino; identification of agents that protect against inflammatory injury to neurons) TT Brain, disease (amyloid angiopathy, plaque component from; identification of agents that protect against inflammatory injury to neurons) IT Nervous system (amyotrophic lateral sclerosis, plaque component from; identification of agents that protect against inflammatory injury to neurons) TΤ Macrophage (and macrophage precursor cells and macrophage-like cells; identification of agents that protect against inflammatory injury to neurons) TΤ Monocyte (and monocyte precursor cells and monocyte-like cells; identification of agents that protect against inflammatory injury to neurons) ĨΤ Nucleic acids RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process) (biosynthesis; identification of agents that protect against inflammatory injury to neurons) TΤ Cat (Felis catus) Dog (Canis familiaris) Guinea pig (Cavia porcellus) Primate Rabbit Rodent Swine (brain; identification of agents that protect against inflammatory injury to neurons) ITNerve, disease (death; identification of agents that protect against inflammatory injury to neurons) IT Nervous system (degeneration; identification of agents that protect against inflammatory injury to neurons) TT Amyloidosis (hereditary, cerebral hemorrhage type, Dutch type, plaque component from; identification of agents that protect against inflammatory injury to neurons) IT Brain (hippocampus; identification of agents that protect against inflammatory injury to neurons) IT Anti-Alzheimer's agents Antiparkinsonian agents Astrocyte Brain Cell morphology

IT

TT

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Imaging

Drug delivery systems Drug screening Nucleic acid amplification (method) Structure-activity relationship Translation, genetic (identification of agents that protect against inflammatory injury to neurons) Peptides, biological studies RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (identification of agents that protect against inflammatory injury to neurons) Glycoproteins, general, biological studies RL: BPR (Biological process); BSU (Biological study, unclassified); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); PROC (Process) (identification of agents that protect against inflammatory injury to neurons) Human immunodeficiency virus 1 (infection; identification of agents that protect against inflammatory injury to neurons) Signal transduction, biological (inhibitors; identification of agents that protect against inflammatory injury to neurons) Nerve, disease (injury; identification of agents that protect against inflammatory injury to neurons) Lipoproteins RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (low-d., acetylated, saporin conjugates; identification of agents that protect against inflammatory injury to neurons) Ion channel RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (membrane ion gradients; identification of agents that protect against inflammatory injury to neurons) Metabolism (metabolic function loss; identification of agents that protect against inflammatory injury to neurons) Neuroglia (microglia, and microglia precursor cells and microglia-like cells; identification of agents that protect against inflammatory injury to neurons) Respiration, animal (mitochondrial; identification of agents that protect against inflammatory injury to neurons) Liposomes Microspheres (mononuclear phagocyte or plaque component adhered to; identification of agents that protect against inflammatory injury to neurons) Cytokines Enzymes, biological studies Lipoproteins Proteins, general, biological studies Radicals, biological studies RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(mononuclear phagocyte-plaque component complex; identification of

protect against inflammatory injury to neurons)

(mononuclear phagocyte release of; identification of agents that

agents that protect against inflammatory injury to neurons) TT Phagocyte (mononuclear, plaque component complex formation; identification of agents that protect against inflammatory injury to neurons) IT Cell death Nerve (neuron; identification of agents that protect against inflammatory injury to neurons) IT Cytoprotective agents (neuroprotectants; identification of agents that protect against inflammatory injury to neurons) TΤ Toxicity (neurotoxicity; identification of agents that protect against inflammatory injury to neurons) IT Toxins RL: ADV (Adverse effect, including toxicity); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation) (neurotoxins; identification of agents that protect against inflammatory injury to neurons) IT Dyes (penetration; identification of agents that protect against inflammatory injury to neurons) TT Amines, biological studies Amines, biological studies RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (phenolic; identification of agents that protect against inflammatory injury to neurons) IT Human immunodeficiency virus (plaque component from infection with; identification of agents that protect against inflammatory injury to neurons) Alzheimer's disease IT Down's syndrome Multiple sclerosis Parkinson's disease (plaque component from; identification of agents that protect against inflammatory injury to neurons) IT Proteins, specific or class RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation) (plaque; identification of agents that protect against inflammatory injury to neurons) IΤ Mitochondria (respiration; identification of agents that protect against inflammatory injury to neurons) IT Proteins, specific or class RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (saporins, conjugates, with acetylated LDL; identification of agents that protect against inflammatory injury to neurons) IT Brain, disease (senile plaque; identification of agents that protect against inflammatory injury to neurons) IT Brain, disease (spongiform encephalopathy, plaque component from; identification of agents that protect against inflammatory injury to neurons) IT Brain, disease (stroke, plaque component from; identification of agents that protect against inflammatory injury to neurons) IT Antigens RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(surface; identification of agents that protect against inflammatory

injury to neurons)

IT Nerve

(toxicity; identification of agents that protect against inflammatory injury to neurons)

IT Injury

(trauma, plaque component from; identification of agents that protect against inflammatory injury to neurons)

IT Scavenger receptors

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(type II; identification of agents that protect against inflammatory injury to neurons)

IT Drug delivery systems

(unit doses; identification of agents that protect against inflammatory injury to neurons)

IT Amyloid

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

 $(\beta$ -; identification of agents that protect against inflammatory injury to neurons)

IT 89-00-9, Quinolinic acid 77006-27-0

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (identification of agents that protect against inflammatory injury to neurons)

- IT107761-42-2, Glycopeptide (human clone 9-110 amyloid A4 107015-83-8 peptide moiety) 107761-42-2D, Glycopeptide (human clone 9-110 amyloid A4 peptide moiety), modified 109770-29-8, 1-28-Glycopeptide (human clone 9-110 amyloid A4 peptide moiety) 118427-80-8 131438-79-4 131580-10-4 131602-53-4 133605-53-5 144409-98-3 146621-55-8 152286-31-2 155178-13-5D, carboxyl-terminal variants 176390-02-6 176390-21-9 190436-05-6 205437-69-0 205454-00-8 205437-73-6 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study) (identification of agents that protect against inflammatory injury to neurons)
- IT 50-02-2, Dexamethasone 51-61-6, Dopamine, biological studies 51-67-2, Tyramine 51-67-2D, Tyramine, derivs. 53-86-1, Indomethacin 54-05-7, 54-05-7D, Chloroquine, derivs. 60-18-4, Tyrosine, Chloroquine biological studies 64-86-8, Colchicine 70-18-8, Glutathione, biological studies 104-14-3, Octopamine 145-63-1, Suramine 446-72-0, 477-84-9, Damnacanthal 556-02-5, D-Tyrosine 949-67-7, 1080-06-4, L-Tyrosine methyl ester L-Tyrosine ethyl ester 1406-18-4, 4357-95-3, L-Tyrosine  $\beta$ -naphthylamide 6292-90-6, Vitamin E L-Tyrosine butyl ester 6384-92-5, NMDA 7662-51-3, L-Tyrosine hydrazide 9001-05-2, Catalase 10182-84-0, Diphenyl iodonium 16874-12-7, L-Tyrosine tert-butyl ester 16874-12-7D, Tyrosine tert-butyl ester, 23210-56-2, Ifenprodil 42406-77-9, L-Tyrosine mono- and di-iodinated benzyl ester 76326-31-3, AP5 77086-22-7, MK801 85797-13-3, AP7 125441-04-5, L-Tyrosine allyl ester 90237-02-8, GAMS 118876-58-7 125441-05-6 150403-88-6 154447-36-6, LY294002 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(identification of agents that protect against inflammatory injury to neurons)

IT 9001-92-7, Protease 9005-49-6, Heparin sulfate, biological studies 9050-30-0, Heparan sulfate

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(identification of agents that protect against inflammatory injury to neurons)

IT 141176-92-3P

RL: PUR (Purification or recovery); PREP (Preparation)

(identification of agents that protect against inflammatory injury to neurons)

IT 72-57-1, Trypan blue

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (identification of agents that protect against inflammatory injury to neurons)

IT 80449-02-1, Tyrosine kinase

RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; identification of agents that protect against inflammatory injury to neurons)

IT 50-99-7, Glucose, biological studies

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(metabolism; identification of agents that protect against inflammatory injury to neurons)

IT 9012-36-6, Sepharose 9014-76-0, Sephadex

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (mononuclear phagocyte or plaque component adhered to; identification of agents that protect against inflammatory injury to neurons)

IT 10102-43-9, Nitric oxide, biological studies

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(mononuclear phagocyte release of; identification of agents that protect against inflammatory injury to neurons)

IT 56-65-5, Adenosine triphosphate, biological studies

RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)

(production; identification of agents that protect against inflammatory injury to neurons)

IT 141256-43-1, Antichymotrypsin

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

 $(\alpha\text{--}; identification of agents that protect against inflammatory injury to neurons)$ 

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD RE

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IT 176390-02-6

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study) (identification of agents that protect against inflammatory injury to neurons)

RN 176390-02-6 HCAPLUS

CN L-Phenylalanine, L-histidyl-L-histidyl-L-glutaminyl-L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

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PAGE 1-B

L45 ANSWER 20 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1998:137096 HCAPLUS

DN 128:305262

ED Entered STN: 09 Mar 1998

TI Measurement of peptide aggregation with pulsed-field gradient nuclear magnetic resonance spectroscopy

AU Mansfield, Shawn L.; Jayawickrama, Dimuthu A.; Timmons, Jeffery S.; Larive, Cynthia K.

CS Department of Chemistry, University of Kansas, Lawrence, KS, 66045, USA

SO Biochimica et Biophysica Acta (1998), 1382(2), 257-265 CODEN: BBACAQ; ISSN: 0006-3002

PB Elsevier Science B.V.

DT Journal

LA English

CC 6-3 (General Biochemistry)

AB Interactions between hydrophobic patches in proteins are often a driving force for denaturation and aggregation. The aggregation of the  $\beta\text{-amyloid}$  peptide fragment, VHHQKLVFFAEDVGSNK ( $\beta(12\text{-}28))$ , has been investigated in aqueous solution at low pH. This peptide contains a

central

hydrophobic patch spanning residues 17-21. Diffusion coeffs. measured with pulsed-field gradient NMR as a function of peptide solution concentration were

used to assess the extent of aggregation. Following the hypothesis that hydrophobic interactions are an important driving force in the aggregation of this peptide at low pH, a non-aggregating analog of the  $\beta$ (12-28) peptide,  $[Gly19,20]\beta(12-28)$  was synthesized. In the [Gly19,20] $\beta$ (12-28) peptide, the replacement of the two phenylalanine residues disrupts the hydrophobic interactions which drive the aggregation of  $\beta(12-28)$ . The diffusion coefficient of the [Gly19,20] $\beta(12-28)$ peptide is invariant over the concentration range studied and provides a good estimate of the monomeric diffusion coefficient of  $\beta(12-28)$ . A second peptide analog was synthesized in which the phenylalanine at position 20 was replaced with a cysteine residue. The disulfide-linked dimer, ([Cys20] $\beta$ (12-28))2, was formed upon air oxidation of this peptide. diffusion coefficient of the ([Cys20] $\beta$ (12-28))2 peptide was measured and used to estimate the diffusion coefficient of the  $\beta(12-28)$  dimer. Using the monomeric and dimeric diffusion coeffs. measured for the glycine and cysteine analogs, the concentration dependence of the  $\beta(12\text{-}28)$  diffusion coefficient was found to be consistent with a monomer-dimer aggregation model. beta amyloid peptide aggregation monomer dimer Aggregation Diffusion Hydrophobicity Self-association (β-amyloid peptide and analogs monomer-dimer aggregation studied by pulsed-field gradient NMR spectroscopy) Peptides, biological studies RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process) (\( \beta - amyloid \) peptide and analogs monomer-dimer aggregation studied by pulsed-field gradient NMR spectroscopy) 107015-83-8 RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process) (β-amyloid peptide and analogs monomer-dimer aggregation studied by pulsed-field gradient NMR spectroscopy) 206198-56-3P 206198-57-4P 206281-19-8P RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)  $(\beta\text{-amyloid peptide} \text{ and analogs monomer-dimer aggregation studied}$ by pulsed-field gradient NMR spectroscopy) RE.CNT THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD 55 (1) Ackland, C; J Chromatogr 1991, V540, P187 HCAPLUS (2) Agarawalla, S; Protein Sci 1996, V5, P270 (3) Akiyoshi, K; Macromolecules 1993, V26, P3062 HCAPLUS (4) Altieri, A; J Am Chem Soc 1995, V117, P7566 HCAPLUS (5) Anon; United States Pharmacopia XXII 1990, P1590 (6) Ayalon, A; Angew Chem, Int Ed Engl 1995, V34, P8106 (7) Batlle, A; J Chromatogr 1967, V28, P82 HCAPLUS (8) Battacharyya, P; Anal Chem 1978, V50, P1462 (9) Brackman, J; Langmuir 1991, V7, P46 HCAPLUS (10) Brochon, J; Anal Chem 1993, V65, P1028 HCAPLUS (11) Callaghan, P; Aust J Phys 1984, V37, P359 HCAPLUS (12) Castano, E; Biochem Biophys Res Commun 1986, V141, P782 HCAPLUS (13) Chen, C; AIChE J 1995, V41, P1015 HCAPLUS (14) Dingley, A; J Biomol NMR 1995, V6, P321 HCAPLUS (15) Esler, W; Biochemistry 1996, V35, P13914 HCAPLUS (16) Everhart, C; J Magn Reson 1982, V48, P466 HCAPLUS (17) Fields, G; J Phys Chem 1992, V96, P3974 HCAPLUS (18) Fraser, P; Biophys J 1991, V60, P1190 HCAPLUS (19) Goldwitz, B; J Pharm Sci 1973, V62, P115 HCAPLUS

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- IT 206198-57-4P

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)

 $(\beta$ -amyloid peptide and analogs monomer-dimer aggregation studied by pulsed-field gradient NMR spectroscopy)

RN 206198-57-4 HCAPLUS

CN L-Alanine, L-lysyl-L-leucyl-L-valyl-L-phenylalanyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

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DN
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     Entered STN: 14 Aug 1997
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     Peptide binding the KLVFF sequence of amyloid \beta
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     Nordstedt, Christer; Naslund, Jan; Thyberg, Johan; Tjernberg, Lars O.;
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     Karolinska Innovations Ab, Swed.; Nordstedt, Christer; Naslund, Jan;
PΑ
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US 2002094957
                ECLA
                       C07K005/08A1B; C07K005/08B; C07K005/08C; C07K005/08H1;
                       C07K005/10A1B; C07K005/10B; C07K005/10C; C07K005/10H;
                       C07K014/47A3; G01N033/68V2
US 2004157781
                ECLA
                       C07K005/08A1B; C07K005/08B; C07K005/08C; C07K005/08H1;
                       C07K005/10A1B; C07K005/10B; C07K005/10C; C07K005/10H;
                       C07K014/47A3; G01N033/68V2
AB
    The invention relates to compds. of formula which are of interest especially
for
     inhibition of polymerization of amyloid β peptide, as model substances for
     synthesis of amyloid \beta peptide-ligands, as tool for the
     identification of other organic compds. with similar functional properties
     and/or as ligands for detection of amyloid deposits using E.G. positron
    emission topog. (PET). KLVFF, an amyloid β sequence, was identified
    and was shown to be required for amyloid fibril formation. Ligands
    binding to KLVFF may inhibit fibril formation and could be of therapeutic
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value in treatment of Alzheimer's disease.
ST
     beta amyloid polymn KLVFF sequence inhibitor
IT
     Alzheimer's disease
        (peptide binding the KLVFF sequence of amyloid β and inhibition of
        amyloid polymerization)
IT
     Peptides, biological studies
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic
     use); BIOL (Biological study); PREP (Preparation); USES (Uses)
        (peptide binding the KLVFF sequence of amyloid \beta and inhibition of
        amyloid polymerization)
IT
     Amyloid
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (\beta-; peptide binding the KLVFF sequence of amyloid \beta and
        inhibition of amyloid polymerization)
     64533-15-9P 134649-29-9P
IT
                                138647-36-6P
                                                141684-15-3P
     152647-23-9P 153247-40-6P 176390-00-4P
     176390-01-5P 176390-02-6P 176390-03-7P
     176390-04-8P 176390-05-9P 176390-06-0P
                                               176390-07-1P
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                                               176390-11-7P
     176390-12-8P
                    176390-13-9P 176390-14-0P
                                                 176390-15-1P
     176390-16-2P
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                                   176390-18-4P 176390-19-5P
     176390-20-8P
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                                                                  176390-24-2P
     176390-25-3P
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     189064-06-0P
                    192699-30-2P 192699-31-3P
                                                 192699-32-4P
     192699-33-5P
                    192699-34-6P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic
     use); BIOL (Biological study); PREP (Preparation); USES (Uses)
        (peptide binding the KLVFF sequence of amyloid β and inhibition of
        amyloid polymerization)
IT
     134649-29-9P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic
     use); BIOL (Biological study); PREP (Preparation); USES (Uses)
        (peptide binding the KLVFF sequence of amyloid \beta and inhibition of
        amyloid polymerization)
RN
     134649-29-9 HCAPLUS
CN
     L-Phenylalanine, L-valyl-L-histidyl-L-histidyl-L-glutaminyl-L-lysyl-L-
     leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)
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PAGE 1-A

PAGE 1-B

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L45 ANSWER 22 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
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- AN 1997:458252 HCAPLUS
- DN 127:107496
- ED Entered STN: 23 Jul 1997
- TI Controlling amyloid  $\beta$ -peptide fibril formation with protease-stable ligands. [Erratum to document cited in CA127:32334]
- AU Tjernberg, Lars O.; Lilliehook, Christina; Callaway, David J. E.; Naslund, Jan; Hahne, Solveig; Thyberg, Johan; Terenius, Lars; Nordstedt, Christer
- CS Lab. Biochem. Mol. Pharmacol., Sect. Drug Dependence Res., Dep. Clinical Neurosci., Karolinska Hosp., Stockholm, S-171 76, Swed.
- SO Journal of Biological Chemistry (1997), 272(28), 17894 CODEN: JBCHA3; ISSN: 0021-9258
- PB American Society for Biochemistry and Molecular Biology
- DT Journal
- LA English
- CC 14-10 (Mammalian Pathological Biochemistry)
   Section cross-reference(s): 1
- AB The micrograph in Fig. 5 did not reproduce adequately. Fig. 5 is

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reproduced in better quality.
     erratum Alzheimer amyloid fibril peptide ligand; Alzheimer amyloid fibril
ST
     peptide ligand erratum
     Combinatorial library
IT
     Molecular association
     Molecular modeling
     Protein motifs
        (D-pentapeptides effect on β-amyloid peptide fibril formation
        (Erratum))
     Peptidomimetics
ΙT
        (D-pentapeptides effect on \beta-amyloid peptide fibril formation in
        relation to (Erratum))
     Structure-activity relationship
IT
        (amyloid peptide-binding; of peptide homologs (Erratum))
IT
     Organelle
        (fibril; D-pentapeptides effect on \beta-amyloid peptide fibril
        formation (Erratum))
TT
     Peptides, biological studies
     RL: BAC (Biological activity or effector, except adverse); BPR (Biological
     process); BSU (Biological study, unclassified); PRP (Properties); BIOL
     (Biological study); PROC (Process)
        (pentapeptides; D-pentapeptides effect on β-amyloid peptide fibril
        formation (Erratum))
IT
     131438-79-4
     RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
        (D-pentapeptides effect on β-amyloid peptide fibril formation
        (Erratum))
ŢŢ
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                   190775-16-7
                                 190775-17-8
                                                190775-18-9
                                                              190775-19-0
     190775-20-3
                   190775-21-4
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     190775-50-9
                   190775-51-0
                                 190775-52-1
                                               190775-53-2
     RL: BAC (Biological activity or effector, except adverse); BPR (Biological
     process); BSU (Biological study, unclassified); PRP (Properties); BIOL
     (Biological study); PROC (Process)
        (D-pentapeptides effect on β-amyloid peptide fibril formation
        (Erratum))
IT
     190775-13-4
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (peptide homolog association with (Erratum))
TT
     153247-40-6D, peptides-containing
     RL: BAC (Biological activity or effector, except adverse); BPR (Biological
     process); BSU (Biological study, unclassified); PRP (Properties); BIOL
     (Biological study); PROC (Process)
        (\beta-amyloid peptide association with (Erratum))
IT
     190775-14-5
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (β-amyloid peptide association with (Erratum))
IT
     153247-40-6D, peptides-containing
     RL: BAC (Biological activity or effector, except adverse); BPR (Biological
     process); BSU (Biological study, unclassified); PRP (Properties); BIOL
     (Biological study); PROC (Process)
        (β-amyloid peptide association with (Erratum))
RN
     153247-40-6 HCAPLUS
CN
     L-Phenylalanine, L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX
     NAME)
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L45 ANSWER 23 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1997:318416 HCAPLUS

DN 127:32334

ED Entered STN: 19 May 1997

TI Controlling amyloid  $\beta$ -peptide fibril formation with protease-stable ligands

AU Tjerenberg, Lars O.; Lilliehook, Christina; Callawya, David J. E.; Naslund, Jan; Hahne, Solveig; Thyberg, Johan; Terenius, Lars; Nordstedt, Christer

CS Lab. Biochem. Mol. Pharmacol., Sect. Drug Dependence Res., Dep. Clinical Neurosci., Karolinska Hosp., Stockholm, S-171 76, Swed.

SO Journal of Biological Chemistry (1997), 272(19), 12601-12605 CODEN: JBCHA3; ISSN: 0021-9258

PB American Society for Biochemistry and Molecular Biology

DT Journal

LA English

CC 14-10 (Mammalian Pathological Biochemistry)
 Section cross-reference(s): 1

AB The authors have previously shown that short peptides incorporating the sequence KLVFF can bind to the ~40-amino acid residue Alzheimer amyloid  $\beta$ -peptide (A $\beta$ ) and disrupt amyloid fibril formation. Here, it is shown that KLVFF binds stereospecifically to the homologous sequence in A $\beta$  (i.e. A $\beta$ 16-20). Mol. modeling suggests that association of the two homologous sequences leads to the formation of an atypical anti-parallel \( \beta \)-sheet structure stabilized primarily by interaction between the Lys, Leu, and C-terminal Phe. By screening combinatorial pentapeptide libraries exclusively composed of D-amino acids, several ligands with a general motif containing phenylalanine in the second position and leucine in the third position were identified. Ligands composed of D-amino acids were not only capable of binding AB but also prevented formation of amyloid-like fibrils. These ligands are protease-resistant and may thus be useful as exptl. agents against amyloid fibril formation in vivo.

ST Alzheimer amyloid fibril peptide ligand

IT Structure-activity relationship

(amyloid peptide-binding; of peptide homologs)

IT Organelle

(fibril; D-pentapeptides effect on  $\beta$ -amyloid peptide fibril formation)

IT Peptides, biological studies

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)

(pentapeptides; D-pentapeptides effect on  $\beta$ -amyloid peptide fibril formation)

IT Combinatorial library
Molecular association
Molecular modeling
Protein motifs

(D-pentapeptides effect on β-amyloid peptide fibril formation) IT Peptidomimetics (D-pentapeptides effect on  $\beta$ -amyloid peptide fibril formation in relation to) IT 190775-13-4 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (peptide homolog association with) IT 153247-40-6D, peptides-containing RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process) (β-amyloid peptide association with) IT190775-14-5 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (β-amyloid peptide association with) IT 131438-79-4 RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (D-pentapeptides effect on  $\beta$ -amyloid peptide fibril formation) IT 190775-15-6 190775-16-7 190775-17-8 190775-18-9 190775-19-0 190775-20-3 190775-21-4 190775-22-5 190775-23-6 190775-24-7 190775-25-8 190775-26-9 190775-27-0 190775-28-1 190775-29-2 190775-30-5 190775-31-6 190775-32-7 190775-33-8 190775-34-9 190775-35-0 190775-36-1 190775-37-2 190775-38-3 190775-39-4 190775-40-7 190775-41-8 190775-42-9 190775-43-0 190775-44-1 190775-45-2 190775-46-3 190775-47-4 190775-48-5 190775-49-6 190775-50-9 190775-51-0 190775-52-1 190775-53-2 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process) (D-pentapeptides effect on  $\beta$ -amyloid peptide fibril formation) RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD RE (1) Benet, L; Goodman and Gilman's The Pharmacological Basis of Therapeutics 1996, P3 (2) Buxbaum, J; Proc Natl Acad Sci U S A 1990, V87, P6003 HCAPLUS (3) Camilleri, P; FEBS Lett 1994, V341, P256 HCAPLUS (4) Citron, M; Neuron 1996, V16, P171 (5) Frank, R; Tetrahedron 1992, V48, P9217 HCAPLUS (6) Games, D; Nature 1995, V373, P523 HCAPLUS (7) Ghanta, J; J Biol Chem 1996, V271, P29525 HCAPLUS (8) Glenner, G; Biochem Biophys Res Commun 1984, V120, P885 HCAPLUS (9) Goate, A; Nature 1991, V349, P704 HCAPLUS (10) Hsiao, K; Science 1996, V274, P99 HCAPLUS (11) Hughes, S; Proc Natl Acad Sci U S A 1996, V93, P2065 HCAPLUS (12) Iversen, L; Biochem J 1995, V311, P1 HCAPLUS (13) Jarrett, J; Cell 1993, V73, P1055 HCAPLUS (14) Kang, J; Nature 1987, V325, P733 HCAPLUS (15) Levy-Lahad, E; Science 1995, V269, P970 HCAPLUS (16) Levy-Lahad, E; Science 1995, V269, P973 HCAPLUS (17) Lorenzo, A; Proc Natl Acad Sci U S A 1994, V91, P12243 HCAPLUS (18) Masters, C; Proc Natl Acad Sci U S A 1985, V82, P4245 HCAPLUS (19) Mullan, M; Nat Genet 1992, V1, P345 HCAPLUS (20) Nordstedt, C; J Biol Chem 1994, V269, P30773 HCAPLUS (21) Pike, C; J Neurochem 1995, V64, P253 HCAPLUS (22) Pike, C; J Neurosci 1993, V13, P1676 HCAPLUS (23) Rogaev, E; Nature 1995, V376, P775 HCAPLUS (24) Scheuner, D; Nat Med 1996, V2, P864 HCAPLUS (25) Selkoe, D; Annu Rev Cell Biol 1994, V10, P373 HCAPLUS (26) Shearman, M; Proc Natl Acad Sci U S A 1994, V91, P1470 HCAPLUS (27) Sherrington, R; Nature 1995, V375, P754 HCAPLUS

(28) Tamaoka, A; J Biol Chem 1994, V269, P32721 HCAPLUS

- (29) Tegge, W; Biochemistry 1995, V34, P10569 HCAPLUS
- (30) Tjernberg, L; J Biol Chem 1996, V271, P8545 HCAPLUS
- (31) Tomiyama, T; Biochem Biophys Res Commun 1994, V204, P76 HCAPLUS
- (32) Wisniewski, T; Biochem Biophys Res Commun 1991, V179, P1247 HCAPLUS
- (33) Yankner, B; Science 1990, V250, P279 HCAPLUS
- IT 153247-40-6D, peptides-containing

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)

(β-amyloid peptide association with)

RN 153247-40-6 HCAPLUS

CN L-Phenylalanine, L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

- L45 ANSWER 24 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
- AN 1996:748345 HCAPLUS
- DN 126:19332
- ED Entered STN: 21 Dec 1996
- TI Preparation of peptides as modulators of amyloid aggregation
- IN Findeis, Mark A.; Benjamin, Howard; Garnick, Marc B.; Gefter, Malcolm L.; Hundal, Arvind; Kasman, Laura; Musso, Gary; Signer, Ethan R.; Wakefield, James; et al.
- PA Pharmaceutical Peptides Incorporated, USA
- SO PCT Int. Appl., 105 pp.

CODEN: PIXXD2

- DT Patent
- LA English
- IC ICM C07K014-47
  - ICS A61K038-17
- CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1

FAN.CNT 7

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	ΕP	P 815134		B1 20020605			0605									
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		IE,	FI													
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PRAI US 1995-404831 A
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AU 1996-52524 A3
                                 19950314 <--
                                 19950607 <--
                                 19951027
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                         W
                                 19960314 <--
     WO 1996-US3492
                         A3
     AU 1997-42387
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CLASS
 PATENT NO.
              CLASS PATENT FAMILY CLASSIFICATION CODES
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 WO 9628471 ICM
                        C07K014-47
                        A61K038-17
                ICS
 WO 9628471 ECLA C07K014/47A3
US 5817626 ECLA C07K014/47A3
US 5854215 ECLA C07K014/47A3
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                                                                              <--
     Compds. that modulate the aggregation of amyloidogenic proteins or
     peptides are disclosed. The modulators of the invention can promote
     amyloid aggregation or, more preferably, can inhibit natural amyloid
     aggregation. In a preferred embodiment, the compds. modulate the
     aggregation of natural \beta amyloid peptides (\beta-AP). In a
     preferred embodiment, the \beta amyloid modulator compds. of the
     invention are comprised of an AB aggregation core domain and a
     modifying group coupled thereto such that the compound alters the
     aggregation or inhibits the neurotoxicity of natural \beta amyloid
     peptides when contacted with the peptides. Furthermore, the modulators
     are capable of altering natural \beta-AP aggregation when the natural
     \beta-APs are in a molar excess amount relative to the modulators.
     Pharmaceutical compns. comprising the compds. of the invention, and
     diagnostic and treatment methods for amyloidogenic diseases using the
     compds. of the invention, are also disclosed. These peptide compds. are
     bound to natural \beta-amyloid peptides to facilitate diagnosis of a
     β-amyloidogenic disease, in particular Alzheimer's disease, and are
     useful for treating a disorder associated with amyloidosis including, e.g.
     familial amyloid polyneuropathy or cardiomyopathy, isolated cardiac
     amyloid, systemic senile amyloidosis, scrapie, bovine spongiform
     encephalopathy, and Creutzfeldt-Jakob disease. Thus,
     N-biotinyl-DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVV-OH
     (N-biotinyl-\beta-AP1-40), prepared by the solid phase synthesis using a
     Nα-Fmoc-based protection strategy and Fmoc-Val-Wang resin, at 1%
     markedly inhibited aggregation of the natural \beta-amyloid peptide
     (\beta-AP1-40).
ST
     peptide prepn modulator amyloid aggregation; diagnosis amyloidogenic
     disease Alzheimer disease; amyloidosis assocd disorder; familial amyloid
    polyneuropathy cardiomyopathy treatment peptide; isolated cardiac amyloid
     treatment peptide; systemic senile amyloidosis treatment peptide; scrapie
     treatment peptide; bovine spongiform encephalopathy treatment peptide;
     Creutzfeldt Jakob disease treatment peptide
IT
    Brain, disease
     Prion diseases
        (Creutzfeldt-Jakob; preparation of peptides as modulators of amyloid
        aggregation for treating amyloidosis-associated disorders)
IT
    Deafness
```

Urticaria

(Muckle-Wells syndrome in familial Mediterranean Fever and familial amyloid nephropathy; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)

IT Diagnosis

(agents, for Alzheimer's disease; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)

IT Heart, disease

Heart, disease

(amyloidosis, isolated; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)

IT Nervous system (disease, Gerstmann-Straussler syndrome; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)

IT Amyloidosis

Amyloidosis

(familial Mediterranean fever, with Muckle-Wells syndrome; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)

IT Fever and Hyperthermia

Fever and Hyperthermia

(familial Mediterranean, with Muckle-Wells syndrome; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)

IT Kidney, disease

(familial amyloid nephropathy with Muckle-Wells syndrome and fibrinogen-associated hereditary renal amyloidosis; preparation of peptides

modulators of amyloid aggregation for treating amyloidosis-associated disorders)

IT Heart, disease

(familial amyloidotic cardiomyopathy; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)

IT Amyloidosis

as

(familial amyloidotic polyneuropathy, type IV; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)

IT Amyloidosis

(familial amyloidotic polyneuropathy; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)

IT Dialysis

( $\bar{\text{h}}$ emodialysis, amyloidosis associated with long term hemodialysis; preparation

of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)

IT Brain, disease

(hemorrhage, hereditary cerebral hemorrhage with amyloidosis of Iceland type; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)

IT Amyloidosis

(hereditary, lysozyme-associated; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)

IT Pancreatic islet of Langerhans

(insulinoma; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)

IT Carcinoma

(medullary, amyloidosis associated with thyroid medullary carcinoma; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)

IT Macroglobulins

RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)

(metabolic disorders, macroglobulinemia, myeloma or

 ${\tt macroglobulinemia-associated}$  amyloidosis; preparation of peptides as  ${\tt modulators}$ 

of amyloid aggregation for treating amyloidosis-associated disorders) IT Multiple myeloma

(myeloma or macroglobulinemia-associated amyloidosis; preparation of peptides

as modulators of amyloid aggregation for treating amyloidosis-associated disorders)

IT Diabetes mellitus

(non-insulin-dependent; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)

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IT
     Nerve, disease
        (polyneuropathy, familial amyloid; preparation of peptides as modulators of
        amyloid aggregation for treating amyloidosis-associated disorders)
IT
     Peptides, preparation
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); USES (Uses)
        (preparation of peptides as modulators of amyloid aggregation for treating
        amyloidosis-associated disorders)
IT
     Amyloid
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     MSC (Miscellaneous); BIOL (Biological study); PREP (Preparation)
        (preparation of peptides as modulators of amyloid aggregation for treating
        amyloidosis-associated disorders)
IT
     Sjogren's syndrome
        (primary localized cutaneous nodular amyloidosis-associated; preparation of
        peptides as modulators of amyloid aggregation for treating
        amyloidosis-associated disorders)
IT
     Amyloidosis
        (primary; preparation of peptides as modulators of amyloid aggregation for
        treating amyloidosis-associated disorders)
IT
     Brain, disease
     Prion diseases
        (scrapie; preparation of peptides as modulators of amyloid aggregation for
        treating amyloidosis-associated disorders)
IT
     Amyloidosis
        (secondary; preparation of peptides as modulators of amyloid aggregation for
        treating amyloidosis-associated disorders)
IT
     Amyloidosis
        (senile, systemic; preparation of peptides as modulators of amyloid
        aggregation for treating amyloidosis-associated disorders)
IT
     Brain, disease
        (spongiform encephalopathy; preparation of peptides as modulators of amyloid
        aggregation for treating amyloidosis-associated disorders)
IT
     Alzheimer's disease
        (treatment and diagnosis; preparation of peptides as modulators of amyloid
        aggregation for treating amyloidosis-associated disorders)
IT
     123529-23-7P 153247-40-6P
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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)

IT 58-85-5, Biotin 64-19-7, Acetic acid, reactions 67-43-6 81-25-4, Cholic acid 40248-63-3, (-)-Menthoxyacetic acid 68858-20-8D, Wang resin-bound 72088-94-9 131438-79-4 183745-73-5 183745-81-5 183745-82-6

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)

IT 153247-40-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)

RN 153247-40-6 HCAPLUS

CN L-Phenylalanine, L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L45 ANSWER 25 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1996:233397 HCAPLUS

DN 124:306542

ED Entered STN: 20 Apr 1996

TI Arrest of β-amyloid fibril formation by a pentapeptide ligand

AU Tjernberg, Lars O.; Naeslund, Jan; Lindqvist, Fredrik; Johansson, Jan;
Karlstroem, Anders R.; Thyberg, Johan; Terenius, Lars; Nordstedt, Christer

CS Laboratory Biochemistry Molecular Pharmacology, Karolinska Hospital, Stockholm, S-171 76, Swed.

SO Journal of Biological Chemistry (1996), 271(15), 8545-8 CODEN: JBCHA3; ISSN: 0021-9258

PB American Society for Biochemistry and Molecular Biology

DT Journal

LA English

CC 1-3 (Pharmacology)

Polymerization of amyloid  $\beta$ -peptide (A $\beta$ ) into amyloid fibrils is a critical step in the pathogenesis of Alzheimer's disease. Here, we show that peptides incorporating a short A $\beta$  fragment (KLVFF; A $\beta$ 16-20) can bind full-length A $\beta$  and prevent its assembly into amyloid fibrils. Through alanine substitution, it was demonstrated that amino acids Lys16, Leu17, and Phe20 are critical for binding to A $\beta$  and inhibition of A $\beta$  fibril formation. A mutant A $\beta$  mol., in which these residues had been substituted, had a markedly reduced capability of forming amyloid fibrils. The present data suggest that residues A $\beta$ 16-20 serve as a binding sequence during A $\beta$  polymerization and fibril formation. Moreover, the present KLVFF peptide may serve as a lead compound for the development of peptide and nonpeptide agents aimed at inhibiting A $\beta$  amyloidogenesis in vivo.

ST pentapeptide amyloidogenesis inhibitor Alzheimer disease

```
Molecular structure-biological activity relationship
IT
        (amyloidogenesis-inhibiting; arrest of \beta-amyloid fibril formation
        by a pentapeptide ligand)
     Peptides, biological studies
IT
     RL: BAC (Biological activity or effector, except adverse); BPR (Biological
     process); BSU (Biological study, unclassified); PRP (Properties); THU
     (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
        (arrest of \beta-amyloid fibril formation by a pentapeptide ligand)
IT
     Mental disorder
        (Alzheimer's disease, arrest of \beta-amyloid fibril formation by a
        pentapeptide ligand)
IT
     Proteins, specific or class
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (amyloid A4, arrest of \beta-amyloid fibril formation by a
        pentapeptide ligand)
IT
     64533-15-9 134649-29-9
                               138647-36-6
                                             141684-15-3
                                                            152647-23-9
     153247-40-6 176390-00-4 176390-01-5
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                                  176390-28-6
                                                176390-29-7
     RL: BAC (Biological activity or effector, except adverse); BPR (Biological
     process); BSU (Biological study, unclassified); PRP (Properties); THU
     (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
        (arrest of \beta-amyloid fibril formation by a pentapeptide ligand)
IT
     134649-29-9
     RL: BAC (Biological activity or effector, except adverse); BPR (Biological
     process); BSU (Biological study, unclassified); PRP (Properties); THU
     (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
        (arrest of \beta-amyloid fibril formation by a pentapeptide ligand)
RN
     134649-29-9 HCAPLUS
CN
     L-Phenylalanine, L-valyl-L-histidyl-L-histidyl-L-glutaminyl-L-lysyl-L-
     leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)
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PAGE 1-B

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L45 ANSWER 26 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
    1995:594478 HCAPLUS
NΔ
DN
    123:977
ED
    Entered STN: 08 Jun 1995
    Peptides for amelioration of amnesia in Alzheimer's disease caused by
ΤI
    deposition of amyloid beta protein
    Roberts, Eugene
IN
PA
    City of Hope, USA
SO
    PCT Int. Appl., 26 pp.
    CODEN: PIXXD2
DT
    Patent
LΑ
    English
IC
    ICM A61K038-00
    ICS C07K005-00; C07K007-00; C07K017-00
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    1-11 (Pharmacology)
FAN.CNT 1
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                                                            19940916 <--
    EP 670731
                      A1 19950913 EP 1994-929818
                                                            19940916 <--
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               ICS
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          ECLA
WO 9508999
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                                                                     <--
US 5470951
              ECLA C07K005/10A1A; C07K005/10C; C07K014/47A3
                                                                     <--
os
    MARPAT 123:977
    Three non-amnestic and non-memory enhancing peptides, Asp-Phe-Phe-Val-Gly,
    Gln-Phe-Val-Gly, and Ala-Ile-Phe-Thr, that block the amnestic effects of
    \beta-(12-28), a peptide homologs to amyloid \beta protein (A\beta),
    are disclosed. The invention relates to amelioration of amnesia and other
    neurotoxicity in Alzheimer's disease (AD) caused by deposition of \ensuremath{\mathtt{A}\beta}
    and, therefore, relates to attenuation of the disease process and
    consequential improvement of the quality of life for the individuals
```

suffering from AD. The effects of a series of peptides on the amnestic effects of  $\beta(12-28)$  in mice were determined

ST Alzheimer disease amnesia treatment peptide

IT Amnesia

(peptides for amelioration of amnesia in Alzheimer's disease caused by deposition of amyloid  $\boldsymbol{\beta}$  protein)

IT Peptides, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(peptides for amelioration of amnesia in Alzheimer's disease caused by deposition of amyloid  $\beta$  protein)

IT Mental disorder

(Alzheimer's disease, peptides for amelioration of amnesia in Alzheimer's disease caused by deposition of amyloid  $\beta$  protein)

IT Proteins, specific or class

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (amyloid A4, peptides for amelioration of amnesia in Alzheimer's disease caused by deposition of amyloid  $\beta$  protein)

IT 2131-06-8 2577-40-4, Phenylalanyl phenylalanine 3918-94-3, Valyl valine 53932-31-3 64533-12-6 140941-10-2 **153247-40-6** 153247-41-7 153247-43-9 153247-49-5 153247-51-9 163623-31-2 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(peptides for amelioration of amnesia in Alzheimer's disease caused by deposition of amyloid  $\beta$  protein)

IT 153247-44-0 153247-44-0D, esters and amides 153247-48-4

153247-48-4D, esters and amides 153247-50-8 153247-50-8D, esters and amides

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(peptides for amelioration of amnesia in Alzheimer's disease caused by deposition of amyloid  $\beta$  protein)

IT 153247-40-6

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(peptides for amelioration of amnesia in Alzheimer's disease caused by deposition of amyloid  $\boldsymbol{\beta}$  protein)

RN 153247-40-6 HCAPLUS

CN L-Phenylalanine, L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L45 ANSWER 27 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1995:573971 HCAPLUS

DN 122:306561

ED Entered STN: 26 May 1995

TI Use of a topographic receptor model to identify the binding site for amnestic peptides and the design of memory-enhancing drugs

IN Roberts, Eugene

PA City of Hope, USA

SO PCT Int. Appl., 50 pp.

```
CODEN: PIXXD2
DT
     Patent
LΑ
     English
IC
     ICM A61K038-00
     ICS C07K005-00; C07K005-08; C07K005-10
CC
     1-11 (Pharmacology)
FAN.CNT 1
     PATENT NO.
                       KIND
                               DATE APPLICATION NO. DATE
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         RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
    US 5652334 A 19970729 US 1993-117927 19930908 <--
CA 2148452 AA 19950315 CA 1994-2148452 19940908 <--
EP 668776 A1 19950830 EP 1994-928038 19940908 <--
EP 668776 B1 20000412
    EP 668776
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        R: DE, FR, GB
PRAI US 1993-117927 A 19930908 <--
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                        W
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CLASS
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 WO 9507093 ICM A61K038-00
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                       C07K005-00; C07K005-08; C07K005-10
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US 5652334 ECLA C07K005/02A; C07K005/02B; C07K005/02C; C07K005/10B <--
    A topog. model useful to design and synthesize memory-enhancing substances
AB
     is disclosed. Administration of substances designed by this method to
    enhance memory in mammals, including humans, is disclosed. Such
     substances include peptides having the amino acid sequence Val-Phe.
    Compds. with potential uses as memory enhancers were tested by their
     effects on learning an avoidance response. The structure and activity
    relationships were used to determine the topog. for the binding sites for these
     compds. A potential memory-enhancing substance is designed on the basis
    of these data.
ST
    amnestic peptide receptor topog model; memory enhancing drug receptor
    model
IT
    Peptides, biological studies
    RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
        (amnestic; use of topog. receptor model to identify binding site for
       amnestic peptides and design of memory-enhancing drugs)
IT
    Quantitative structure-activity relationship
        (memory-affecting; use of topog. receptor model to identify binding
       site for amnestic peptides and design of memory-enhancing drugs)
IT
    Memory, biological
    Simulation and Modeling, biological
        (use of topog. receptor model to identify binding site for amnestic
       peptides and design of memory-enhancing drugs)
IT
    Molecular structure-biological activity relationship
        (memory-affecting, use of topog. receptor model to identify binding
       site for amnestic peptides and design of memory-enhancing drugs)
IT
    67412-83-3 99473-67-3 99896-85-2 107015-83-8 112163-49-2
    134649-29-9
                 153247-41-7 153247-46-2 153247-53-1
    153287-77-5
                 163350-37-6 163350-38-7 163350-39-8 163350-40-1
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    RL: BAC (Biological activity or effector, except adverse); BSU (Biological
    study, unclassified); PRP (Properties); BIOL (Biological study)
        (memory enhancing activity of; use of topog. receptor model to identify
       binding site for amnestic peptides and design of memory-enhancing
       drugs)
```

IT 153247-47-3

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(peptides containing, as memory enhancers; use of topog. receptor model to identify binding site for amnestic peptides and design of memory-enhancing drugs)

IT 134649-29-9

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study) (memory enhancing activity of; use of topog. receptor model to identify

binding site for amnestic peptides and design of memory-enhancing drugs)

drugs)

RN 134649-29-9 HCAPLUS

CN L-Phenylalanine, L-valyl-L-histidyl-L-histidyl-L-glutaminyl-L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

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1994:131262 HCAPLUS
AN
DN
     120:131262
ED
     Entered STN: 19 Mar 1994
     Topography of a binding site for small amnestic peptides deduced from
ΤI
     structure-activity studies: relation to amnestic effect of amyloid \beta
    protein
     Flood, James F.; Roberts, Eugene; Sherman, Mark A.; Kaplan, Bruce E.;
ΑU
     Morley, John E.
     Geriatr. Res. Educat. clin. Cent. (GRECC), St. Louis, MO, 63106, USA
CS
     Proceedings of the National Academy of Sciences of the United States of
SO
     America (1994), 91(1), 380-4
     CODEN: PNASA6; ISSN: 0027-8424
DT
     Journal
     English
LΑ
CC
     14-10 (Mammalian Pathological Biochemistry)
     Section cross-reference(s): 1
AB
     Four peptides homologous to amyloid β protein containing the Val-Phe-Phe
     (VFF) sequence administered intracerebroventricularly after training
     caused amnesia for footshock active avoidance training in mice. Results
     with VFF and other peptides containing VFF or portions there of were used to
     generate a topog. map for a hypothetical binding surface for amnestic
    peptides, termed Z. Effects on retention of footshock active avoidance
     training were rationalized in terms of fit to Z, making possible design of
     potential memory-modulating peptidic and nonpeptidic substances. Three
    peptides that neither improved nor impaired retention blocked the amnestic
     effects of \beta-(12-28), a peptide homologous to amyloid \beta protein,
     opening the way to development of substances that can antagonize the
     neurotoxic effects of amyloid β protein on neural structures and thus
     attenuate symptoms and progression of Alzheimer disease.
ST
     amyloid beta protein amnestic peptide
IT
    Amnesia
    Memory, biological
        (small peptides related to amyloid \beta protein mediation of,
        structure-activity in)
IT
     Proteins, specific or class
     RL: BIOL (Biological study)
        (amyloid A4, small amnestic peptides in relation to, structure-activity
        in)
ΙT
    Molecular structure-biological activity relationship
        (memory-affecting, small peptides related to amyloid \beta protein in)
                             3918-90-9
IT
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        (amnestic effect of, structure-activity in, amyloid \beta protein in
        relation to)
IT
    153247-40-6
     RL: PRP (Properties)
        (amnestic effect of, structure-activity in, amyloid \beta protein in
        relation to)
RN
     153247-40-6 HCAPLUS
    L-Phenylalanine, L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX
CN
    NAME)
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L45
    ANSWER 29 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
    1993:671728 HCAPLUS
AN
DN
    119:271728
    Entered STN: 25 Dec 1993
ED
    Preparation of pseudopentapeptides with immunomodulating activity
ΤI
    Degraw, Joseph I.; Almquist, Ronald; Hiebert, Charles; Smith, R. Lane;
IN
    Uchida, Itsuo
PA
    Japan Tobacco, Inc., Japan
    PCT Int. Appl., 201 pp.
SO
    CODEN: PIXXD2
DT
    Patent
LA
    English
IC
     ICM C07K005-02
     ICS C07K007-02; A61K037-02; C07K015-00
CC
     34-3 (Amino Acids, Peptides, and Proteins)
     Section cross-reference(s): 1, 15
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                                          CA 1992-2094822
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    EP 556405
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WO 9304080
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                ICS
                       C07K007-02; A61K037-02; C07K015-00
OS
    MARPAT 119:271728
AB
    Thymopentin (thypentin) analogs, e.g. R-AA1-AA2-AA3-AA4-AA5-R1 [AA1 = L-
    or D-Arg; AA2 = optionally N-C1-6 alkylated L- or D-basic amino acid
    residue, a neutral/nonarom. amino acid residue, or Pro; AA3 = L- or D-Asp
    or Glu optionally esterified with C1-6 alkyl; AA4 = L- or
    D-neutral/nonarom. amino acid residue; AA5 = optionally N-C1-6 alkylated
    L- or D-neutral/nonarom. amino acid residue (wherein one or more H's of
     its aromatic portion can be substituted by NO2 or halo) or L- or
    D-neutral/nonpolar/large/nonarom. amino acid residue; R = C1-6 acyl,
    arylsulfonyl, alkylsulfonyl, arylalkylsulfonyl, alkoxycarbonyl; R1 = OH,
    NR2R3 (wherein R2, R3 = H, C1-6 alkyl), OR4 (R4 = C1-6 alkyl); wherein at
    least one of the linkages AA1-AA2, AA2-AA3, AA3-AA4, and AA4-AA5 is a
    modified peptide linkage selected from COCH2, CH(OH)CH2, and CH2NH and the
    remaining linkages are CONH or CONMe], useful for the treatment of
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autoimmune and infectious diseases (e.g. arthritis), are prepared Thus,

coupling of a Grignard reagent PhCH2CH(CH:CH2)CH2MgBr (preparation given) with N-trityl-L-valine 2-mercaptopyridine ester (preparation given) in THF at 50-60° for 2 h followed by N-deprotection with p-MeC6H4SO3H in MeCN and N-protection with (Me3CO)2CO in CH2Cl2 containing Et3N gave N-tert-butoxycarbonyl-6-amino-7-methyl-3-benzyl-1-octen-5-one. Oxidation of the latter with RuO2.xH2O/NaIO4 in aqueous acetone gave 5-N-tertbutoxycarbonylamino-6-methyl-2-benzyl-4-oxoheptanoic acid which was bound to a Merrifield chloromethyl resin and underwent solid-phase peptide coupling with Boc-Lys(ClZ)-Asp(OcHex)-OH (ClZ = 2-chlorobenzyloxycarbonyl, cHex = cyclohexyl) (preparation given) and Boc-Arg(Tos)-OH using DCC and hydroxybenzotriazole to give, after deprotection and resin cleavage, H-Arg-Lys-Asp-Val(k)Phe-OH [wherein (k) indicates the linkage COCH2 as a replacement for CONH] (I). In a competitive binding assay, I at 10-3 and 10-4 M in vitro reduced the mean total count of tritiated thymopentin bound to CEM cells from 3,078 cpm (in the absence of a competitor) to 844 cpm vs. 1,150 cpm for non-radiolabeled thymopentin. The peptide analogs in vitro also increased the release of cyclic GMP in CEM cells, the production of Thy-1 antigens in spleen cells of nu/nu mice, and the serum half-life in mouse and human serum. pseudopentapeptide prepn immunomodulating activity; autoimmune treatment pseudopentapeptide; infectious disease treatment pseudopentapeptide; thymopentin thypentin analog prepn immunomodulator Immunostimulants Immunosuppressants (pseudopentapeptide thymopentin analogs) Autoimmune disease Infection (treatment of, pseudopentapeptide thymopentin analogs for) Inflammation inhibitors (antiarthritics, pseudopentapeptide thymopentin analogs) Peptides, preparation RL: SPN (Synthetic preparation); PREP (Preparation) (penta-, pseudo-, thymopentin analogs, preparation of, as immunomodulator) 72210-37-8P 151012-26-9P 151012-27-0P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and reaction of, in preparation of immunomodulating pseudopentapeptide thymopentin analog) 151011-32-4P 151011-34-6P 151011-36-8P 151011-37-9P 151011-39-1P 151011-41-5P 151011-43-7P 151011-45-9P 151011-47-1P 151011-49-3P 151011-51-7P 151011-53-9P 151011-54-0P 151011-55-1P 151011-57-3P 151011-59-5P 151011-61-9P 151011-62-0P 151011-64-2P 151011-65-3P 151011-67-5P 151011-69-7P 151011-70-0P 151011-71-1P 151011-72-2P 151011-73-3P 151011-74-4P 151011-75-5P 151011-76-6P 151011-77-7P 151036-34-9P 151036-36-1P 151036-37-2P 151121-46-9P 151121-48-1P 151121-50-5P 151121-52-7P 151121-54-9P 151121-56-1P 151121-58-3P 151121-60-7P 151121-62-9P 151121-64-1P 151121-66-3P 151121-67-4P 151121-69-6P 151121-71-0P 151121-72-1P 151121-75-4P 151121-77-6P RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of, as immunomodulator) 962-39-0P, L-Phenylalanine benzyl ester 63628-63-7P 78314-61-1P 80514-64-3P 80622-02-2P 82068-75-5P 89760-63-4P 103143-66-4DP, MBHA resin-bound 139033-47-9P 151011-78-8P 151011-79-9P 151011-80-2P 151011-81-3P 151011-82-4P 151011-83-5P 151011-84-6P 151011-85-7DP, Resin-bound 151011-86-8DP, Resin-bound 151011-87-9P 151011-88-0P 151011-89-1DP, Resin-bound 151011-89-1P 151011-90-4P 151011-91-5P 151011-92-6P 151011-93-7P 151011-94-8P 151011-95-9P 151011-99-3DP, Resin-bound 151011-96-0P 151011-97-1DP, Resin-bound 151012-00-9P 151012-01-0P 151012-02-1P 151012-03-2P 151012-04-3P

151012-07-6P

151012-15-6P

151012-11-2DP, Resin-bound

151012-08-7P

151012-16-7P

151012-11-2P

151012-09-8P

151012-17-8P

151012-12-3P

st

IT

IT

IT

IT

IT

IT

TT

151012-05-4P

151012-10-1P

151012-13-4P

151012-06-5P

151012-14-5P

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151012-18-9P 151012-19-0P 151012-20-3P 151012-21-4P 151012-25-8P 151036-38-3P 151036-39-4P 151036-40-7P 151036-41-8P 151036-42-9P 151121-73-2P
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RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of, as intermediate for immunomodulating pseudopentapeptide thymopentin analog)

ΙT 50-00-0, Formaldehyde, reactions 56-41-7, L-Alanine, reactions 72-18-4, L-Valine, reactions 76-83-5, Trityl chloride 115-11-7, Isobutylene, reactions 334-88-3, Diazomethane 541-16-2, Di-tert-butyl 542-69-8, 1-Iodobutane 542-92-7, Cyclopentadiene, reactions malonate 1155-64-2 1738-78-9 2177-63-1 2637-34-5, 2-Mercaptopyridine 2812-46-6, L-Proline tert-butyl ester 3392-10-7 6638-79-5, N,O-Dimethylhydroxylamine hydrochloride 6921-34-2, Benzylmagnesium chloride 13734-34-4D, resin-bound 13734-34-4D, p-methylbenzhydrylamine resin-bound 13734-41-3 13836-37-8 14611-34-8 15761-38-3 21657-35-2D, resin-bound 24424-99-5, Di-tert-butyl dicarbonate 30794-77-5, 1,4-Dibromobutene 31950-55-7, 1-Bromo-2-methyl-3-butene 50774-73-7, 4-Methyl-3-bromomethyl-1-pentene 54613-99-9 57096-11-4 73821-95-1, N-tert-Butoxycarbonyl-L-aspartic acid β-cyclohexyl ester 73995-27-4 107304-39-2 151012-22-5, L-Aspartic acid benzhydryl ester 151012-23-6

RL: RCT (Reactant); RACT (Reactant or reagent) (reaction of, in preparation of immunomodulating pseudopentapeptide thymopentin analog)

IT 151011-70-0P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of, as immunomodulator)

RN 151011-70-0 HCAPLUS

CN L-Phenylalanine, N-[N-[N-[N2-[2-amino-5-[(aminoiminomethyl)amino]pentyl]-L-lysyl]-L- $\alpha$ -aspartyl]-L-valyl]-, (S)- (9CI) (CA INDEX NAME)

L45 ANSWER 30 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1991:427112 HCAPLUS

DN 115:27112

ED Entered STN: 27 Jul 1991

TI Amnestic effects in mice of four synthetic peptides homologous to amyloid  $\beta$  protein from patients with Alzheimer disease

AU Flood, James F.; Morley, John E.; Roberts, Eugene

CS VA Med. Cent., St. Louis, MO, 63106, USA

SO Proceedings of the National Academy of Sciences of the United States of America (1991), 88(8), 3363-6
CODEN: PNASA6; ISSN: 0027-8424

DT Journal

LA English

CC 14-10 (Mammalian Pathological Biochemistry)

AB Immediate post-training intracerebroventricular administration of a synthetic peptide homologous to  $\beta$ -protein of brain amyloid, [Gln11] $\beta$ -(1-28), caused amnesia for footshock active avoidance training in mice in a dose-dependent fashion. This effect was specific to memory processing since the peptide did not cause amnesia when injected 24 h after training nor did it disturb storage or retrieval of older memories. Shorter fragments of the amyloid  $\beta$ -protein consisting of

residues 12-28, 18-28, and 12-20 also were amnestic when given intracerebroventricularly, residues 12-20 being least effective. The hippocampus, a brain structure importantly involved in learning and memory, consistently shows severe pathol. changes and deposition of amyloid in patients with Alzheimer disease. Immediate post-training bilateral intrahippocampal injection of [Gln11] $\beta$ -(1-28) produced amnesia at much lower doses than did [Gln11] $\beta$ -(1-28) injected intracerebroventricularly. Thus these exptl. results suggest a possible direct role of amyloid  $\beta$ -protein or fragments thereof in an aspect of the spectrum of cognitive deficit in Alzheimer disease.

ST Alzheimer amyloid beta peptide amnesia

IT Amnesia

(from peptides homologous to amyloid  $\beta\text{-protein}$  of humans with Alzheimer disease)

IT Mental disorder

(Alzheimer's disease, amyloid  $\beta$ -protein from humans with, synthetic peptides homologous to, amnestic effect of)

IT 106686-61-7 107015-83-8 112163-49-2 134649-29-9

RL: PRP (Properties)

(amnestic effect of, as homolog of amyloid  $\beta$ -protein from humans with Alzheimer disease)

IT 134649-29-9

RL: PRP (Properties)

(amnestic effect of, as homolog of amyloid  $\beta$ -protein from humans with Alzheimer disease)

RN 134649-29-9 HCAPLUS

CN L-Phenylalanine, L-valyl-L-histidyl-L-histidyl-L-glutaminyl-L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

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